Some Researches on the Chemistry of Dimethyl Sulfoxide and Related Compounds

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Some Researches on the Chemistry of Dimethyl Sulfoxide and Related Compounds

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INTRODUCTION

Dimethyl sulfoxide (DMSO) is one of the most versatile substances among organic compounds as a highly polar aprotic solvent and a chemical reagent in organic syntheses. As a chemical reagent, DMSO has three different sites for reactions; on sulfur, on oxygent and on methyl groups. The chemical behavior of DMSO can be roughly classified as follows;

(a) Methylsulfinyl carbanion.
(b) Dimethyloxosulfonium methylide.
(c) An oxidant.
(d) Reactions initiated by an acid.
(e) Other reactions.

Equally fascinating as DMSO itself are other closely related reagents derivable from DMSO, especially, methyl sulfoxide ($R-SO-CH_3$) and sulfonium methylide ($R_2S=CH_2$) have potential uses in organic syntheses and commercial uses as detergents. The varied aspects of chemical and physico-chemical behaviors of DMSO and related compounds have been extensively investigated.

Tertiary amine oxides such as trimethylamine oxide and pyridine N-oxide have closely related chemical behaviors to sulfoxides, although nitrogen can not be anticipated to involve 3 d-orbital.

The authors have taken a special interest in the chemistry of DMSO and related compounds and have performed some studies on this subject for the past five years. A variety of new aspects of the chemistry obtained by the authors are presented in the following sections.

I. The Reaction of Dimethyl Sulfoxide with Some Aromatic Compounds in the Presence of Sulfuric Acid.[1]

The protonation of the oxygen atom of $>\overset{\oplus}{S}-\overset{\ominus}{O}$ bond with strong mineral or organic acid leaves the formally positive sulfur atom open for facile nucleophilic attack.

The acid-catalyzed rearrangement of sulfoxide is known as Pummerer rearrangement. Although the reaction was known for many years, the mechanistic aspects have been studied in detail only more recently and some valuable synthetic applications have been reported. DMSO as an oxidant has many attractive features as follows; (1), the high yields and low temperatures required for the reaction, (2), success with this reagent where others fail or create complications. For example, the facile oxidation-reduction between sulfoxide and sulfide was

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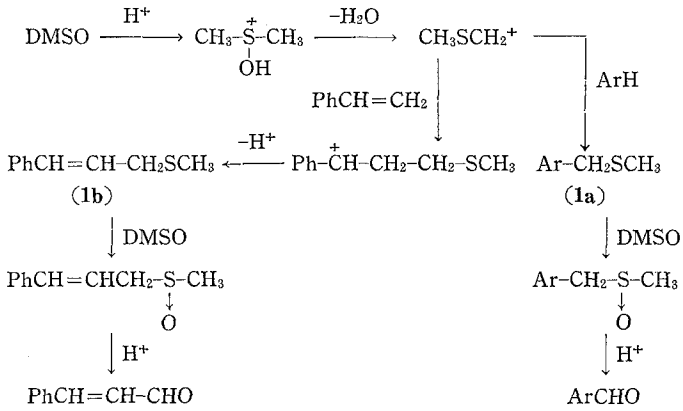
applied to the synthesis of sulfoxides by DMSO as an oxidant.[2] The literatures of these reactions have been reviewed.[3,4]

DMSO was decomposed by sulfuric acid under heating to dimethyl sulfide, dimethyl disulfide and formaldehyde[5] and we found that methylene-bis-benzamide (62% yield) was isolated from the reaction mixture of DMSO, benzonitrile and sulfuric acid even at 80°C.

When sulfuric acid-DMSO mixture was used in the presence of aromatic compounds, a combination of reactions described above would be expected to occur, and the authors found that this was the case.

Methylthiomethyl cation derived from DMSO and sulfuric acid was reacted with some aromatic compounds such as styrene, anisole and naphthalene to give methylthiomethyl derivatives (**1**).



The sulfides **1** were oxidized to sulfoxides by DMSO and the sulfoxides underwent Pummerer rearangement to give aldehydes in the same media. The products were isolated and identified, for example, cinnamaldehyde, *o*- and *p*-methoxy benzaldehyde (10% yield) and α-naphthaldehyde (1% yield) were obtained from styrene, anisole and naphthalene, respectively.

The product distribution and yield were dependent upon the reaction conditions (molar ratio of reagents, temperature).

The results obtained from the reaction mixture of DMSO, styrene and sulfuric acid are shown in Table 1.

Table 1. Reaction of Styrene with DMSO.

Product	Bp. (°C/mm)	Yield (%)
Recovered styrene		40.3
Acetophenone		0.02- 0.04
α-Phenylethyl alcohol		0.01- 0.04
Methyl α-phenylethyl sulfide	91- 92/2	6.1
Cinnamaldehyde	97- 98/5	0.01- 8
Methyl cinnamyl sulfide	126-128/8	1.1 -15.1
1, 3-Diphenylbutene-1	147-148/3	24

Methyl α-phenylethyl sulfide (2) was obtained in 12% yield by the reaction of styrene with dimethyl sulfide in sulfuric acid.

$$PhCH{=}CH_2 \xrightarrow{H^+} Ph{-}\overset{+}{C}H{-}CH_3 \xrightarrow{CH_3SCH_3} Ph{-}\underset{{}^+SMe_2}{CH}{-}CH_3 \longrightarrow Ph{-}\underset{SCH_3}{CH}{-}CH_3 \quad (2)$$

p, *p*′-Dimethoxydiphenylmethane, α, α'-dinaphthylmethane and methylene-bis-benzamide were obtained by the jointing reaction of each aromatic compound with HCHO derived from the decomposition of DMSO by sulfuric acid.

Dimerization of styrene in DMSO or dimethyl sulfide in the presence of sulfuric acid yielded only 1, 3-diphenylbutene-1.

II. The Oxidation of Halides by Dimethyl Sulfoxide or Amine Oxides in the Presence of Epoxides.[6]

The oxidation of alkyl- and aralkyl halides by DMSO or amine oxides is a remarkable selective oxidation. Some examples of the oxidation by DMSO are as follows:

$ArCH_2Br$, $ArCOCH_2Br$, $BrCH_2COOR$, $ArCH_2OTs$, AlkylOTs, $(PhOCH_2)_2CHOTs$, Alkyl-I, $R_2CHOCOCl$, $ArCOCH_2ONO_2$, RCH_2N_2Cl, Epoxide, Carbene, $ArCH_2OH$, RSH, RSR, PR_3, $R_2PS(OH)$, $(RCH_2OH+DCC+H^+)$, $RCH_2OH+(RCO)_2O$, $RCH_2ONa+Me_2SOMe\cdot BF_4$, $RSCl+ArCH_2SCH_3$.

The mechanism of these DMSO oxidations is probably as follows.[7,8]

Compounds having active hydrogen such as phenacyl bromide.

$$RCH_2X + CD_3SOCD_3 \longrightarrow RCH_2\overset{+}{O}S(CD_3)_2 \quad (X^-)$$

$$\downarrow -DX$$

$$R{-}CH{-}O \quad (H,\ S^+,\ \bar{C}D_2,\ CD_3)$$

$$RCHO + CD_3SCD_2H \longleftarrow$$

Compounds having no active hydrogen.

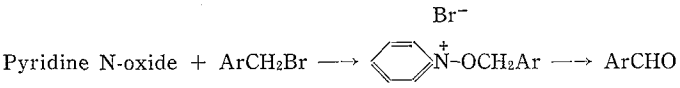
$$RCH_2X + DMSO \longrightarrow R{-}CH(H){-}O{-}\overset{+}{S}Me_2\ (X^-) \longrightarrow RCHO + CH_3SCH_3 + HX$$

This mechanism predicts that secondary compounds (R_2CHX) should be oxidizable to ketones, and this is the case.

Similar oxidations can also be carried out with amine oxides.

R_2CHX, R_2CHOTs, $(R_2CHCO)_2O$, Epoxide, Carbene, BR_3, PX_3, PR_3, $P(OR)_3$, S_8, RSH, RSR, RSCl, PhNHNHPh, Hydroquinone, RCHBrCOOH, SO_2.

The mechanism of the amine oxide oxidation is analogous to that of DMSO.



(3)

The intermediate 3 could be isolated quantitatively and the treatment of 3 with base gave aldehyde.[9]

1, 2-Epoxy-3-phenoxypropane was used as non-alkaline scavenger for hydrogen bromide in the oxidation of bromoacetic acid ester by DMSO[10], but Hunsberger and his co-worker did not find the generality of epoxide as acid scavenger in the oxidation of halides by DMSO.

The authors found that epoxides were very effective base in the oxidation of halides by DMSO or amine oxides. For example, benzaldehyde (yield, 82-87%) and α, α'-dichloroisopropanol (yield, 62-66%) were isolated in the oxidation of benzyl chloride by pyridine N-oxide or DMSO in the presence of epichlorohydrin, while only a trace amount of benzaldehyde could be obtained in the absence of epichlorohydrin under the same condition.

When a mixture of 1-chloromethylnaphthalene (4), DMSO and epichlorohydrin was treated at 150°C for 5 minutes, 1-naphthaldehyde (5, yield, 54%) was isolated and 24% of 4 was recovered. On the other hand, sodium bicarbonate was used as acid acceptor under the same condition in place of epichlorohydrin, only 26% of 5 could be isolated.

The results obtained are shown in Table 2.

Table 2. Oxidation of Halides by Pyridine N-oxide or DMSO.

Halide	Yield (%) of carbonyl compound		Chlorohydrin	Yield (%) of chlorohydrin	
	Pyridine N-oxide	DMSO		Pyridine N-oxide	DMSO
$C_6H_5CH_2Cl$	82	87	Dichloroisopropanol	66	62
	12	19	Phenylethylene chlorohydrin	16	25
	6	6.5	Chlorobutanol	12	7.7
p-Cl-$C_6H_4CH_2Cl$	51	74	Dichloroisopropanol	48	65
p-NO_2-$C_6H_4CH_2Cl$	23	45	〃	45	68
$C_{10}H_7$-α-CH_2Cl	48	59	〃	46	70
n-$C_{12}H_{25}Cl$	trace	11	〃	trace	49
n-$C_{12}H_{25}Br$	38	···	α-Chloro-α'-bromo isopropanol	24	···
n-$C_6H_{13}Br$	···	84	〃	···	40
cyclo-$C_6H_{11}Br$	28	28	〃	0.8	16

The oxidation of alkyl chlorides was difficult, while that of alkyl bromides was easily proceeded.

Chlorohydrins derived from mono-substituted epoxides were mostly RCH(OH)-CH_2Cl. This result would suggest that epoxides eliminate halide anion from the

bulky intermediates, that is, ammonium or sulfonium salt. Later, Nerdel and Buddrus reported that epoxides were effective base in the formation of dichlorocarbene from chloroform.[11]

Epichlorohydrin was the most effective epoxide as halide anion acceptor.[12]

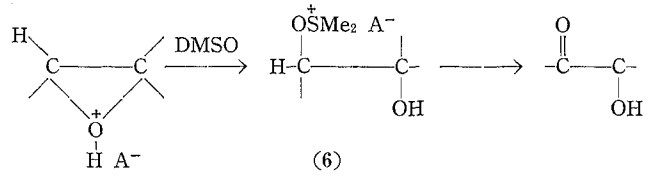
III. The Oxidation of Epoxides by Amine Oxides[13]

It is already known that the oxidation of epoxides by DMSO with boron trifluoride as catalyst at 90–100°C gives α-ketoalcohols.[14]

The authors have found that the α-ketoalcohol was obtained in fairly good yield (46%) from the reaction mixture of styrene oxide and DMSO at 150°C for 15 hrs without catalyst, and also cyclopentene-1-aldehyde (3% yield) was isolated from the reaction of DMSO and cyclohexene oxide, besides the expected α-ketoalcohol.

Later, Tsuji reported that the oxidation can also be effected without BF_3 if air is passed through the reaction mixture or if a catalytic amount of *t*-butyl hydroperoxide is present and suggested that the BF_3-catalyzed reaction is ionic but oxygen- or hydroperoxide-catalyzed one is free radical,[15] while Santosusso and Swern substantiated that the oxidation is not a free radical one but acid-catalyzed ionic one.[16]

They suggested the following mechanism, in which an alkoxysulfonium salt (6) is the key intermediate, from the evidence for the presence of an intermediate obtained by examination of the NMR spectra of styrene oxide and cyclohexene oxide, respectively, in acidified DMSO.



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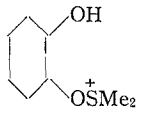
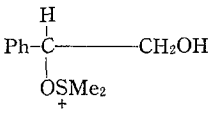


(6a)



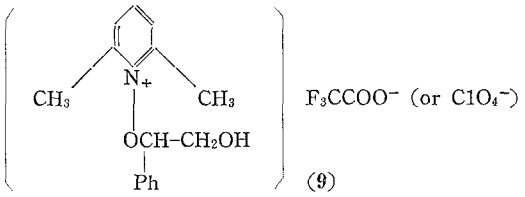
(6b)

The similar oxidation would be expected to occur by the reaction of epoxides with amine oxides, which have analogous reactivity to sulfoxides, and the authors have found that this was the case. In the reaction of epoxides with pyridine N-oxide or trimethylamine oxide, α-ketoalcohols were also obtained, but main products were the carbonyl compounds which were derived from the oxidative cleavage of the carbon-carbon chain of the epoxide ring.

For example, the following products were identified: phenacyl alcohol (yield 4–11%), benzaldehyde (4–47%) and formaldehyde from styrene oxide; 2-hydroxycyclohexanone (7, 1–14%), cyclopentene-1-aldehyde (8, 3–17%) and a trace amount of adipaldehyde from cyclohexene oxide; acetophenone (17%) and formaldehyde from α-methylstyrene oxide; propionaldehyde (10%) and paraformaldehyde (13%)

from 1, 2-butylene oxide (Table 3). In these reactions, Lewis acid showed no catalytic effects on the oxidation and accelerated the dimerization of epoxides.

The mechanism of the amine oxide oxidation is probably analogous to that of DMSO. Later, Marmer and Swern isolated analytically pure pyridinium salt (**9**) from the reaction mixture of lutidine N-oxide and styrene oxide followed by trifluoroacetic acid or perchloric acid, and suggested that the pyridinium salt **9** is also an intermediate of the oxidation.[17]



(**9**)

The mechanism of the oxidative cleavage of the carbon-carbon chain of the epoxide ring are better explained *via* the electrontransfer as follows.

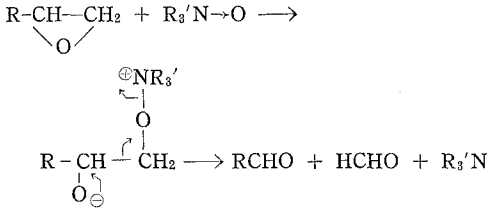


Table 3. Oxidation of Epoxides.

Epoxide	Amine oxide	Solvent	Product	Yield (%)
Cyclohexene-	Pyridine	None	8	14
			7	17
			Adipaldehyde	trace
Cyclohexene-	Trimethylamine	$CHCl_3$	8	1
			7	3
Styrene-	Trimethylamine	$CHCl_3$	Phenacyl alcohol	11
Styrene-	Pyridine	$CHCl_3$	Phenacyl alcohol	5
			Benzaldehyde	4
Styrene-	Pyridine	None	Phenacyl alcohol	5
			Benzaldehyde	32
Styrene-	Pyridine	$ClCH_2CH_2Cl$	Benzaldehyde	47
α-Methylstyrene-	Pyridine	None	Acetophenone	17

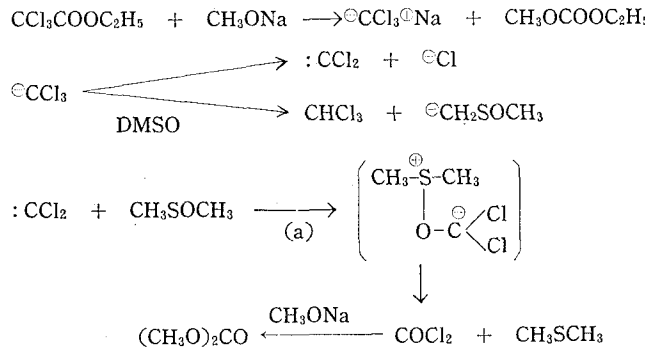
IV. The Oxidation of Carbenes by Dimethyl Sulfoxide[18]

Pyridine N-oxide can serve as a useful species for donating oxygen to carbene under suitable reaction conditions.[2] DMSO is also a selective oxidant and the mechanism of the oxidation is similar to that of amine oxides. We wish to report the oxidation of some carbenes by DMSO to the corresponding carbonyl

compounds.

In the case of dichlorocarbene, the products are expected to be phosgene and dimethyl sulfide. Dimethyl sulfide was identified as $(Me_2S)_2 \cdot 3HgCl_2$,[19] while phosgene was converted into dimethyl carbonate in the presence of sodium methoxide. The reaction was carried out by adding sodium methoxide to a cold DMSO solution of ethyl trichloroacetate. After standing for one hour at ice-cooled temperature, the mixture was poured into ice-water and extracted with ether. Vapor phase chromatographic analysis (v. p. c.) of the extract indicated the yields of the products and recovered starting material to be as follows; dimethyl sulfide (20%), dimethyl carbonate (17%), methyl ethyl carbonate (33%), chloroform (38 %) and ethyl trichloroacetate (8%). The five components were identified by comparison of thier IR, NMR and v. p. c. with authentic samples after separation of each component by v. p. c. It was found that methyl ethyl carbonate underwent transesterification to dimethyl carbonate to the extent of 7% under the reaction conditions described above, although the two carbonates were mostly hydrolysed to sodium salts. This is one of the reasons that the combined yield of chloroform and dimethyl carbonate was higher than that of methyl ethyl carbonate.

The mechanism of the reaction is probably as follows.



The chloroform is presumably formed through the deprotonation of DMSO by the trichloromethyl anion. Step (a) corresponds to the reaction of dichlorocarbene with pyridine N-oxide.[20,21]

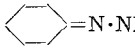
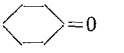
Other carbenes prepared by alkaline cleavage of tosylhydrazones[22,23,24] were also oxidized by DMSO to the corresponding ketones or aldehyde.

The tosylhydrazone was dissolved in DMSO and sodium methoxide was added to the solution. The mixture was heated with stirring at 100~166° in nitrogen atmosphere. The reaction mixture (except cyclohexanone tosylhydrazone) began

to turn wine-red at about 100°. The carbonyl compounds of the products were compared with authentic specimens by v. p. c., IR and semicarbazones. The results obtained are shown in Table 4. Dimethyl sulfide was also isolated in yields comparable to those of the corresponding carbonyl compounds.

In the decomposition of acetophenone and benzophenone tosylhydrazones, the corresponding azines were isolated in 10% and 6% yields, respectively, besides the carbonyl compounds. The yields of the carbonyl compounds were found to drop rapidly if the reaction time is longer than that shown in Table 4.

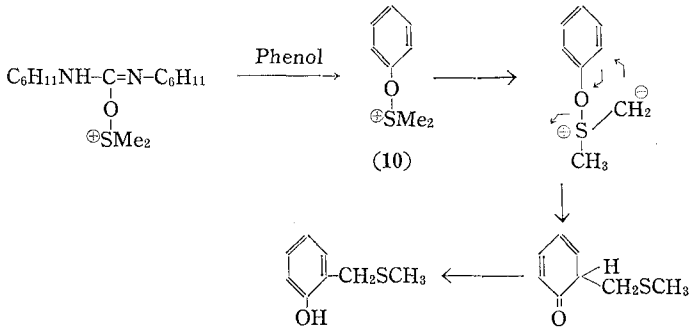
Table 4. Alkaline Cleavage of Tosylhydrazones in DMSO.

Tosylhydrazone	(mole)	Temperature	Time (min)	Product	Yield
$C_6H_5-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}=N\cdot NH\cdot Ts$	(0.052)	100~160°	15	$C_6H_5COCH_3$	46%
$C_6H_5-\underset{\displaystyle C_6H_5}{\overset{\displaystyle |}{C}}=N\cdot NH\cdot Ts$	(0.0286)	100~150°	10	$C_6H_5COC_6H_5$	67%
 $=N\cdot NH\cdot Ts$	(0.0352)	100~166°	18	 $=O$	12%
$C_6H_5\cdot CH=N\cdot NH\cdot Ts$	(0.0365)	100~133°	10	C_6H_5CHO	40%

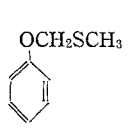
For example, the yield of acetophenone was only 0.8% when the reaction mixture of acetophenone (10g), DMSO (100g) and sodium methoxide (3g) was heated at 100~160° for 18 minutes. A possible cause for this phenomenon is the reaction between the carbonyl compounds and the methylsulfinyl carbanion.

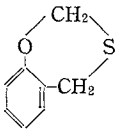
V. The Thiomethoxymethylation of Phenols by Dimethyl Sulfoxide and Acetic Anhydride[29]

Burdon, *et al.*,[25a] and Pfitzner, *et al.*,[25b] have found recently that phenols can be thiomethoxymethylated by DMSO in the presence of dicyclohexylcarbodiimide (DCC) and a proton source.



In this reaction, following products were also isolated.





The authors have found that the same reaction occurred using acetic anhydride instead of DCC at room temperature. Thus, phenol was thiomethoxymethylated to give 2-thiomethoxymethlphenol (**11**) and 2, 6-di(thiomethoxymethyl)phenol (**12**). Phenyl acetate and a small amount of acetate of **11** were also obtained (Table 5).

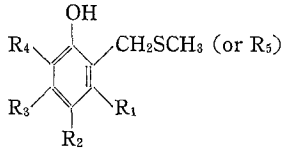
Table 5. Thiomethoxymethylation of Phenol.

Reaction time, hr	Yields of products, %		
	11	**12**	Phenyl acetate
22	19	Trace	10
46	26	0.8	13
84	37	7.2	14
240	31	20	16

o-, *m*-, and *p*-cresol and 2, 4-dimethylphenol gave the corresponding ortho-thiomethoxymethylated products (Table 6).

Weakly acidic phenols such as those in Table 6 gave only 2–16% of phenol acetates, but more acidic phenols like *p*-nitrophenol gave the acetate quantitatively. α-Naphthol gave 71% of α-naphthyl acetate and 12% of β-thiomethoxymethyl-α-naphthylacetate.

Table 6. Thiomethoxymethylphenols.



Phenol	Product		Yield, %	Bp (°C/mm) Mp (°C)
o-Cresol	**13**	$R_4=CH_3$, $R_1=R_2=R_3=H$	25	114–115/5
	14a	$R_2=CH_3$, $R_1=R_3=R_4=H$	36	130/5
p-Cresol	**14b**	$R_4=CH_2SCH_3$, $R_2=CH_3$, $R_1=R_3=H$	9	165–166/4
m-Cresol	**15a**	$R_1=CH_3$, $R_2=R_3=R_4=H$	16	130–132/7
	15b	$R_3=CH_3$, $R_1=R_2=R_4=H$	18	130–132/7
2, 4-Dimethylphenol	**16**	$R_2=R_4=CH_3$, $R_1=R_3=H$	61	130–131/3
2, 6-Dimethylphenol	**17**	$R_2=CH_2SCH_3$, $R_4=R_5=CH_3$, $R_1=R_3=H$	26	136–138/5 43– 45

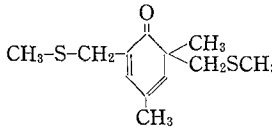
Phenol gave no para- or meta-substituted products. 2, 6-Dimethylphenol which has no available ortho positions gave para-alkylated product (**17**). 2, 6-Di-*t*-butylphenol and 2, 6-di-*t*-butyl-*p*-cresol were recovered unchanged, and in these

cases 45-50% of acetoxymethyl methyl sulfide (**19**) was isolated. On the other hand, the other phenols yielded **19** in less than 5%. *o*-Cresol may be substituted in para position before alkylation of the available ortho position, since desulfurization of the product by Raney nickel gave a small amount of 2, 4-dimethylphenol (0.3%) besides 2, 4, 6-trimethylphenol (0.5%) and 2, 6-dimethylphenol.

Butyric anhydride, polyphosphoric acid, and phosphorus pentoxide can be substituted for acetic anhydride, although the yields are poor.

A mixture of phenol, DMSO, and phosphorus pentoxide gave 1, 3-benzoxathian (14%), **11** (2%), and salicylaldehyde (**20**, 0.5%). Compound **20** may be formed through the Pummerer rearrangement of 2-methylsulfinylmethylphenol which is the oxidation product of **11** by DMSO.[1] *p*-Nitrophenol, using the same reagent, gave 6-nitro-1, 3-benzoxathian (21%).

From the residue after distillation of **16**, a colorless oil (bp. 159~160° c/3 mm) was isolated. Elemental analysis, IR and NMR show the structure of the oil to be **21**.



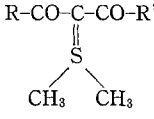
(21)

An alkoxysulfonium cation is postulated as an intermediate in the oxidation of alcohols by acetic anhydride and DMSO.[26] A phenoxysulfonium cation (**22**) may be formed in the reaction of phenol, acetic anhydride, and DMSO, and phenols are thiomethoxymethylated through **22**, which was postulated as an intermediate.[25] Decomposition of a complex of benzene diazonium chloride and zinc chloride in DMSO with expectation that **22** would be formed[27] gave phenol (76%) ; **11** or **12** could not be detected in the reaction mixture.

IV. Stable Sulfur Ylides[28]

It has previously been shown that phenols could be thiomethoxymethylated by DMSO and acetic anhydride.[29] It is of interest whether analogous reaction

Table 7. Stable Sulfur Ylides.



(**23**)

a ; R=CH_3, R'=OCH_3
b ; R=CH_3, R'=OC_2H_5
c ; R=C_6H_5, R'=OC_2H_5
d ; R=R'=CH_3

Active methylene compound	Yield (%)	Mp. (°C)	Bp (°C/mm)	Formula
Methyl acetoacetate	81	115-117	155-157/6	$C_7H_{12}O_3S$
Ethyl acetoacetate	66	62- 63	155-158/5.5	$C_8H_{14}O_3S \cdot 1/2H_2O$
Ethyl benzoylacetate	84	84- 85		$C_{13}H_{16}O_3S$
Acetylacetone	72	167-169		$C_7H_{12}O_2S$
Ethyl acetoacetate	56[a]			

a) Butyric anhydride instead of acetic anhydride

would be occurred using enolizable active methylene compounds. In the course of our examination of this reaction, Gompper and Euchner[30] reported that stable sulfur ylides could be isolated from the reaction mixture of DMSO, acetic anhydride and active methylene compounds. The authors have also found that stable sulfur ylides were obtained from DMSO, acetic (or butyric) anhydride and active methylene compounds such as methyl acetoacetate, ethyl acetoacetate, ethyl benzoylacetate and acetylacetone in high yields (Table 7).

These ylides were too stable to react with carbonyl compounds (**23a** could be recrystallized from benzaldehyde or acetophenone) and stable upon treatment with alkaline aqueous solutions but easily hydrolyzed upon treatment with hot 1 N sulfuric acid. The IR and the NMR spectra of the ylides are shown in Table 8 and 9.

Table 8. IR Spectra of the Ylide. (cm^{-1})

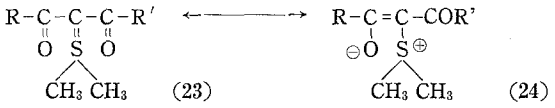
Ylide	ν C=O (R_2C=O)	ν C=O (COOR)	ν OH	Absorption above 3000 cm^{-1}
23 a	1570	1685		3010, 3025
23 b	1540[a]	1680[a]	3390[b]	3010, 3025
23 c	1555	1645		3010, 3025[c]
23 d	1560			3010, 3030

a) Three absorptions at 1575, 1650 and 1680 cm^{-1} in CCl_4.
b) Two absorptions at 3680 cm^{-1} (free OH) and 3460 cm^{-1} (bonded OH) in CCl_4.
c) Aromatic CH at 3040, 3055 and 3080 cm^{-1}.

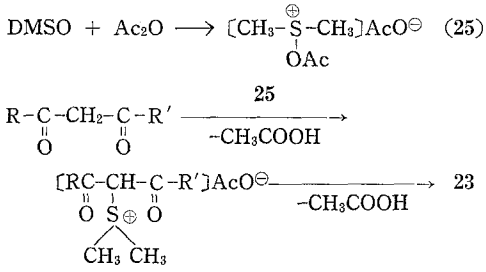
Table 9. NMR Spectra of the Yield. (τ)

Yield	Me_2S	CH_3	CH_2	OH	Solvent
23 a	7.06 (s, 6)	7.78 (s, 3) 8.75 (t, 3)	5.97 (q, 2)	6.43 (s, 1)	CCl_4
23 d	6.99 (s, 6)	7.65 (s, 6)			$CDCl_3$

Resonance effect between **23** and **24** gives rise to a very considerable shift (about 100 cm^{-1}) of the carbonyl frequency and strong absorption at 1600 cm^{-1} in the spectrum of **23d** suggests considerable contribution of the structure **24**.



Some weak and sharp absorptions above 3000 cm^{-1} cannot be explain satisfactorily at present. The mechanism of the reaction is probably as follows



The literatures of this reaction has been reviewed.[31,32]

VII. The Preparation of Alkoxymethyl Acylates[33]

DMSO acid anhydride mixtures are remarkable reagents for the oxidation of alcohols to their corresponding carbonyl derivatives.[26] The generally accepted mechanism as shown below requires that nucleophilic attack of an alcohol on the positively charged sulfur atom of **26** with backside displacement of acetate ion leads to alkoxysulfonium salt **27**, an intermediate of Kornblum oxidation.

$$DMSO + Ac_2O \longrightarrow \underset{(26)}{Me_2\overset{+}{S}OCOCH_3} \xrightarrow{R_2CHOH} \underset{(27)}{R_2CHO\overset{+}{S}Me_2} \longrightarrow R_2CO$$

It is of interest to see whether the reaction of amine oxides with acid anhydride (Polonovski reaction) in the presence of alcohols leads to the oxidation of the alcohols in analogous way to the sulfoxide. We examined this reaction in chloroform using trimethylamine oxide and acid anhydrides in the presence of some alcohols and found that alkoxymethyl acylate was the main product.

n-Butoxymethyl, cyclohexyloxymethyl, benzyloxymethyl and cinnamyloxymethyl acetate were obtained in 26-69% yields. Cyclohexyloxymethyl butyrate and *n*-butoxymethyl benzoate were also obtained in poor yields. Cyclohexyloxymethyl acetate was also isolated from the reaction mixture of N, N-dimethylaniline N-oxide, acetic anhydride and cyclohexanol. The results obtained are shown in Table 10.

Table 10. Alkoxymethyl Acylate.

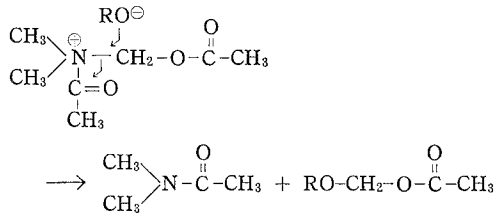
Alkoxymethyl acylate	Bp. (°C/mmHg)	Yield (%)	Yield (%) of alkoxy acylate
cyclo-C_6H_{11}-O-CH_2-$OCOCH_3$	82/ 7	69	12
C_6H_5-CH_2-O-CH_2-$OCOCH_3$	117/ 7	27	59
C_6H_5-CH=CH-CH_2-O-CH_2-$OCOCH_3$	140/ 5	26	54
n-C_4H_9-O-CH_2-$OCOCH_3$	84/35	63	34
cyclo-C_6H_{11}-O-CH_2-OCO-*n*-C_3H_7	105/ 7	16	trace
n-C_4H_9-O-CH_2-OCO-C_6H_5	.....	5	trace

The mechanism of the Polonovski reaction, whereby *tert*-amine oxides containing at least one N-methyl group are converted by acetic anhydride into *sec*-amines and formaldehyde, is probably as follows.[34]

$$\underset{\underset{O}{\downarrow}}{R_2N\text{-}CH_3} + Ac_2O \longrightarrow \underset{\underset{COCH_3}{\diagdown}}{R_2\overset{+}{N}\text{-}CH_2OCOCH_3}, \quad \underset{(29)}{R_2N\text{-}CH_2OCOCH_3}$$
$$(28)$$

$$\xrightarrow{B^-} R_2NCOCH_3 + HCHO + B\text{-}COCH_3$$

The intermediate, **28** or **29**, has not been isolated. Our results reported here substantiate the existance of the intermediate 28 and the formation of alkoxymethyl acylates may be explained as follows.



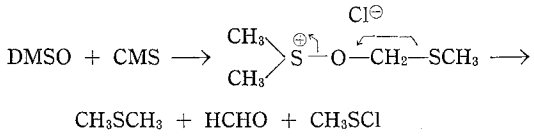
Pyridine N-oxide catalyzed the esterification of alcohols with acetic anhydride but very small amount of cyclohexanone (yield 0.2%) was obtained from the reaction mixture of pyridine N-oxide, acetic anhydride and cyclohexanol.

VIII. The Acid Chloride Catalyzed Reaction of Dimethyl Sulfoxide[35]

The Pummerer rearrangement involving the reaction of DMSO with acid anhydrides[36] or acid chlorides[37] are well known and acyloxymethyl methyl sulfide or chloromethyl methyl sulfide was isolated in high yields. Rätz and Sweeting[38] postulated a mechanism involving several steps to explain the formation of methyl methanethiolsulfonate from DMSO and chloromethyl methyl sulfide (CMS).

$$CMS + 3DMSO \longrightarrow CH_3SO_2SCH_3 + Me_3SCl + HCHO + CH_3SCH_3$$

It was interesting to ascertain the course of this reaction. The authors found that methanesulfenyl chloride, formaldehyde and dimethyl sulfide were obtained from the reaction mixture of DMSO and CMS. With the forementioned information a mechanistic pathway can be postulated which satisfied the empirical observations.



$$CH_3SCH_3 + HCHO + CH_3SCl$$

This reaction is a modification of the well-known oxidation of halides by DMSO and it was found that α-chloro sulfides were generally oxidized by DMSO to carbonyl compounds.[39]

In the trapping experiments of methanesulfenyl chloride with olefins, the adducts were isolated in 39-69% yields (Table 11).

Table 11. Methanesulfenyl Chloride Adducts.

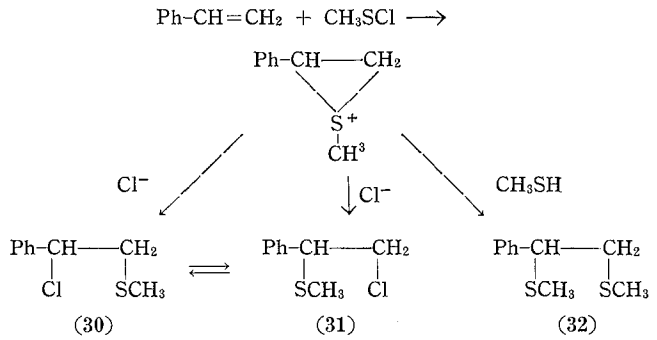
Olefin	Yield (%)
Styrene	45
Acrylonitrile	39
Methyl acrylate	47
Ethyl acrylate	42
Cyclohexene	60
Phenyl acetylene	69

In a similar experiment as above using a variety of acid chlorides, several adducts of styrene were isolated (Table 12).

Table 12. Adducts of Styrene.

Solution	Reagent added	Yield (%) of products			
		30+31	32	Ph-CH(Cl)-CH$_2$Cl	Ph-CH(Cl)-CH$_3$
St. (0.3) DMSO (1.3)	CMS (0.5)	45	7		
St. (0.1) DMSO (0.5)	CH_3SCl (0.1)	56	trace		
St. (0.4) DMSO (2.0)	$POCl_3$ (1.0)	57	6		
St. (0.5) DMSO (0.55) CH_2Cl_2 100 g	$POCl_3$ (1.0)	16	11	13	25
St. (0.5) $POCl_3$ (1.0) CH_2Cl_2 100 g	DMSO (0.55)	trace	trace	24	
St. (0.2) DMSO (1.0)	SO_2Cl_2 (0.1)	38		21	
St. (0.2) CCl_4 50 g	CH_3SCl (0.2)	83			
St. (0.2) PhSOEt (0.2)	CMS (0.2)	30			

The mechanism of the formation of the adducts is probably as follows.



Reaction of sulfenyl chlorides and ketones occurs to give β-keto sulfides, while that of sulfenyl chlorides with α-active methylene sulfides gives sulfonium chloride type intermediates which decomposed to α-chloro sulfides. Thus, acetophenones or benzyl sulfides, when subjected to the action of DMSO and an acid chloride, were oxidized to phenyl glyoxals or benzaldehydes in good yields by the combined reactions described above.[39,40]

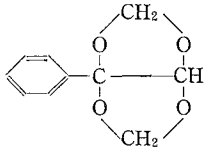
While the reaction of DMSO with CMS is known to give methyl methanethiol-

sulfonate, the essential feature of this reaction was also considered to the reaction of DMSO with methanesulfenyl chloride.

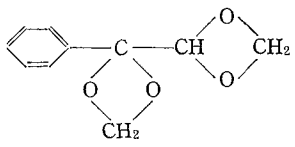
IX. The Oxidation of α-Active Methylene Sulfides by Dimethyl Sulfoxide and an Acid Chloride[39,40]

We wish to report a novel method of oxidation of methyl groups of aromatic methyl ketones with formation of new compounds, 1-aryl-2, 4, 6, 8-tetraoxabicyclo [3, 3, 0] octanes or benzyl sulfides to benzaldehydes using DMSO and certain acid chlorides.

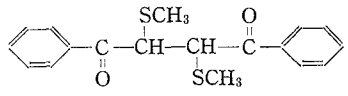
In general the reaction was carried out by adding benzoyl chloride to a solution of an aromatic methyl ketone or a benzyl sulfide in DMSO at 0–15°C. The reaction mixture was kept at room temperature overnight, poured into ice, treated with cold sodium hydroxide aqueous solution and finally extracted with chloroform. Thus, acetophenone underwent oxidation and acetal formation to give 45% of 1-phenyl-2, 4, 6, 8-tetraoxabicyclo[3, 3, 0]octane (**33 a**). A small amount of methyl phenacyl sulfide, phenyl glyoxal, dimethylthiodibenzoylethane (**34**, mp. 208°C), formaldehyde dimethylmercaptal and methyl methanethiolsulfonate were also isolated from the reaction mixture. By substituting benzoyl chloride by acetyl chloride or butyric acid chloride, 12% and 31% of **33 a** were obtained respectively.



33a



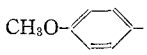
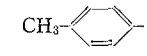
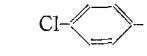
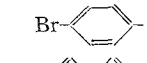
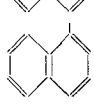
33b



34

The structural assignment of the compound **33 a** was substantiated by elemental analysis, molecular weight, IR, NMR (the chemical shifts are reported

Table 13. 1-Aryl-2, 4, 6, 8-tetraoxabicyclo[3. 3. 0]octanes.

Ar	Yield (%)	Mp (°C) Bp (°C/mm)	N. m. r. in CCl_4
	45	54– 5 100– 2/4	2.36–2.83 (m), 4.58 (s), 4.69 (s) 4.71 (s); 5 : 1 : 2 : 2
	46	98– 9 135–40/5	2.54–3.27 (m), 4.64 (s), 4.70 (s), 4.72 (s), 6.24 (s); 4 : 1 : 2 : 2 : 3
	40	107– 8 116– 8/4	2.76 (q), 4.62 (s), 4.69 (s), 4.71 (s), 7.65 (s); 4 : 1 : 2 : 2 : 3
	41	86– 7 130– 4/6	2.45–2.80 (m), 4.61 (s), 4.68 (s), 4.72 (s); 4 : 1 : 2 : 2
	38	91– 2 139–43/5	2.39–2.77 (m), 4.62 (s), 4.69 (s), 4.73 (s); 4 : 1 : 2 : 2
	36	110– 1	1.88–2.75 (m), 4.51 (s), 4.61 (s), 4.65 (s); 7 : 1 : 2 : 2
	3	165/ 4	1.80–2.83 (m), 4.11 (s), 4.70 (s), 7 : 1 : 4

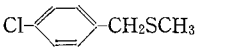
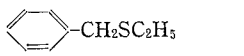
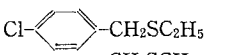
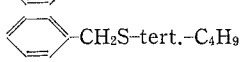
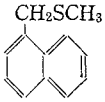
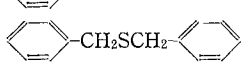
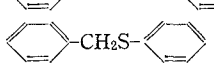
in τ units) and acid hydrolysis to phenyl glyoxal monohydrate and formaldehyde.

It seems probable that the observed singlets of the nmr of the methylene protons originate from an AX pattern and this spectrum supports dioxolane structure of **33 a**.[41] Since all of the five aliphatic protons in structure **33 b** are in a different environment, the structure **33 b** is less possible as an alternative to the structure **33 a** (benzilidene formal was not isolated from the reaction mixture of benzaldehyde, benzoyl chloride and DMSO).

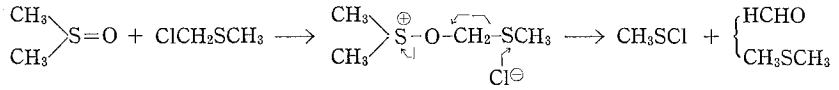
Similar tetraoxabicyclooctanes were obtained from other methyl ketones. On the other hand, propiophenone gave methyl 1-benzoylethyl sulfide in 45% and cyclohexanone gave 2-methylthio-2-cyclohexenone (bp 110°/5, nmr of vinyl proton, a triplet at 3.46) in 27% yield. The nmr spectra of the dioxolanes obtained are shown in Table 13. IR spectra of the dioxolanes show absorptions of dioxolane type ether linkage and a weak and sharp absorption at 2760 cm^{-1}.

The oxidation method is now extended to benzyl sulfides using DMSO and benzoyl chloride.

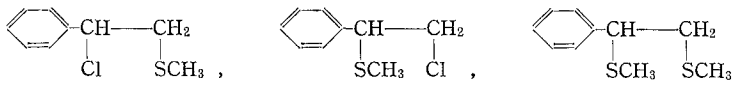
Table 14. The oxidation of benzyl sulfides to benzaldehydes.

Benzyl sulfide	Yield (%) of benzaldehyde	Sulfide	Yield (%) of aldehyde
	85		77
	82		75
	61		89
	74		
	trace		

We have found that this oxidation proceeds *via* α-chloro sulfides which are obtained by chlorination of α-active-methylene sulfides by sulfenyl chloride. Carboxylic acid chlorides are known to react with sulfoxides to give α-chloro sulfides.[37] Chloromethyl methyl sulfide derived from DMSO was further reacted with DMSO[38] to give methanesulfenyl chloride as illustrated below.



In the trapping experiment of methanesulfenyl chloride with styrene, following products were obtained.[42]

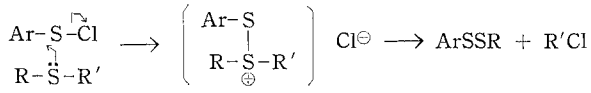


(35) (30%) (36) (15%) (37) (7%)

The above mechanism was substantiated by the fact that the reaction of chloro-

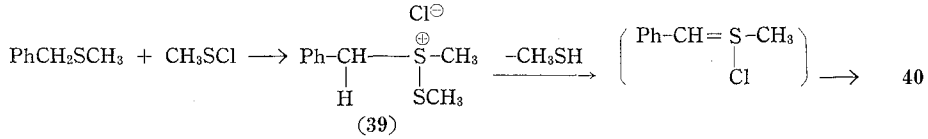
methyl methyl sulfide with ethyl phenyl sulfoxide in the presence of styrene gave a mixture (30%) of **35** and **36**, ethyl phenyl sulfide (89%) and paraformaldehyde (51%). Therefore, the oxidation of methyl ketones or benzyl sulfides is ascribed to the action of methanesulfenyl chloride and DMSO.

α-Chlorobenzyl methyl sulfide[37] was obtained by the reaction of methyl benzyl sulfide with methanesulfenyl chloride. An example of chlorination of sulfides by sulfenyl chlorides has not, to our knowledge, been previously reported. An example of the reaction of 2, 4-dinitrobenzenesulfenyl chloride with monosulfides is that a bimolecular electrophilic attack of the sulfenyl chloride on the monosulfide gives a sulfonium ion type complex (**38**) from which elimination of cationically most stable group occurs to give the products.[43]



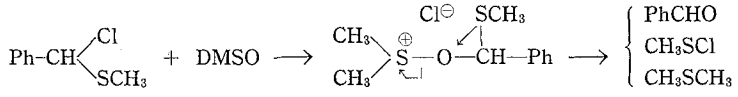
(**38**)

It seems most reasonable to assume that the chlorination of sulfide is effected by abstraction of a benzylic proton of the benzyl sulfide by thiomethoxy ion from the complex (**39**) to give an intermediate[37] which rearrange to α-chlorobenzyl methyl sulfide (**40**).



(**39**)

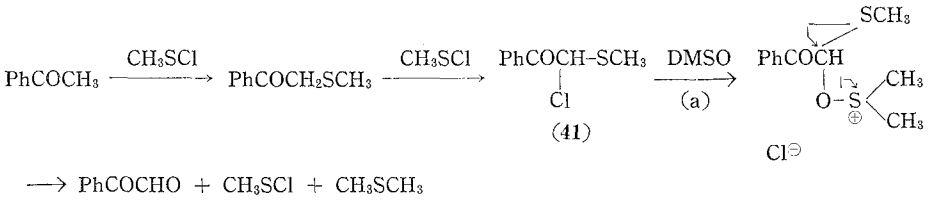
In the formation of sulfonium ion type complex, electron-withdrawing phenyl group deactivated the sulfide sulfur towards electrophilic attack by the sulfenyl chloride (see Table 14). The sulfide **40** in DMSO was oxidized to give benzaldehyde.



Reaction of sulfenyl chlorides and methyl ketones occurs to give β-keto sulfides.[44] The reaction of acetophenone or methyl phenacyl sulfide with methane sulfenyl chloride in carbon tetrachloride gave α-chloro-α-methylthioacetophenone (**41**) besides other comounds. Pure **41** (bp 141/6 mm, obtained from diazoacetophenone and methane sulfenyl chloride) in DMSO was oxidized within one hour to give **33a** (28%), phenyl glyoxal (34%) and benzoylformic acid (30%). The reaction of acetophenone with methanesulfenyl chloride in DMSO gave following products.

	Yield		Yield
33a	4%	PhCOCOOH	trace
PhCOCHO	76%	PhCOOH	trace
$PhCOCH_2SCH_3$	7%		

Thus, following reaction scheme can be suggested as the oxidation sequence of acetophenone.



$\longrightarrow$ $PhCOCHO + CH_3SCl + CH_3SCH_3$

The step (a) corresponds to the reaction of chloromethyl methyl sulfide with DMSO.

The dioxolane **33a** (36%) was isolated from the reaction mixture of phenyl glyoxal, paraformaldehyde and concentrated hydrochloric acid in chloroform, although such simple dioxolane formation was not reported in literature.

Evidence that the oxidation of acetophenones or benzyl sulfides by sulfenyl chloride and DMSO is a general phenomenon is provided by effective catalytic action of other sulfenyl chlorides such as ethanesulfenyl-, *n*-butanesulfenyl- and trichloromethanesulfenyl chloride. For example, the results of the reaction of acetophenone with *n*-butanesulfenyl chloride or trichloromethanesulfenyl chloride in DMSO are shown below.

n-C_4H_9SCl		CCl_3SCl	
Product	Yield (%)	Product	Yield (%)
PhCOCHO	82	$PhCOCH_2SMe_2 \cdot Cl$	51
$(n\text{-}C_4H_9)_2S$	70	PhCOCHO	13
33a	trace	PhCOOH	15
		PhCOCOOH	10
		$PhCOCH_2SCH_3$, **33a**	trace

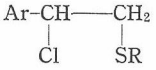
When subjected to the action of chloromethyl methyl sulfide and DMSO, phenacyl chloride was oxidized to phenylglyoxal, while benzyl chlorides gave dimethyl benzyl sulfonium chlorides quantitatively.

X. The Structure of Styrene-Sulfenyl Chloride Adducts and their Reactions[45]

The addition of alkane- and arene-sulfenyl chlorides to unsaturated systems has been received considerable attention. The predominant adduct orientation from these sulfenyl chlorides have been reported to be Markownikoff. In contrast to this generally accepted adduct orientation, it has been shown recently that the initial anti-Markownikoff adducts rearrange to Markownikoff-oriented adducts on standing at ambident temperatures.[42,46,47]

In previous report,[39] we have reported that styrene-methanesulfenyl chloride adducts were isolated from the reaction mixture of styrene, DMSO and chloromethyl methyl sulfide. Our interest in the reaction of sulfenyl chloride addition to styrene stems from the marked difference of the isomer distribution of our result (65 : 35) and that of Mueller and Butler (98 : 2).[42]

We have found that styrene-sulfenyl chloride initial adducts contained no less than 87% of Markownikoff adducts when reacted at low temperature in any solvents except strong acids. These adducts were found to rearrange by heating to the equilibrium mixtures which consisted of ca. 30% of anti-Markownikoff adducts. The rearrangement was acid-catalyzed.


(42)

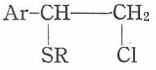
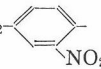

(43)

Table 15. NMR Spectra of 42 and 43.

Ar	R	42		43	
		-CHCl-,	-CH_2SR	-CHSR-,	-CH_2Cl
	CH_3	5.17	6.95 7.06	6.27	
〃	C_2H_5	5.21	6.89 7.06	6.24	
〃	n-C_4H_9	5.21	6.90 7.06	6.24	
〃	CH_3O- 	5.41	6.68 6.82	5.97	6.28 6.40
〃	CH_3- 	5.39	6.64 6.78	5.90	6.30 6.42
〃		5.25	6.56 6.68	5.74	6.22 6.34
〃	Cl- 	5.37	6.66 6.77	5.86	6.31 6.43
〃	NO_2- 	5.22	6.50 6.60	5.51	6.25 6.36
〃	NO_2-  NO_2	4.74[a]	6.12[a] 6.23		
CH_3- 	CH_3	5.11	6.90 7.01	6.20	
Cl- 	CH_3	5.15	6.88 7.02	6.20	

a) in DMSO

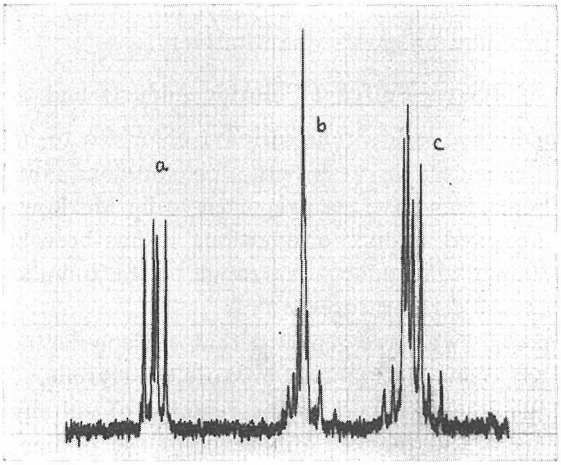


Fig. 1. Styrene-CH_3SCl adducts (100 Mc, in CCl_4).

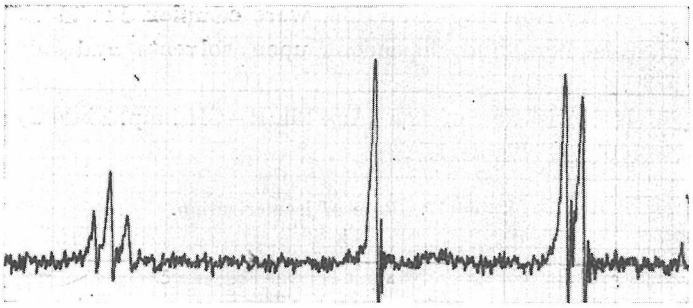


Fig. 2. Styrene-CH_3SCl adducts (100 Mc, in DMSO-D_6).

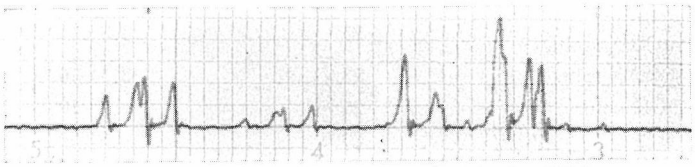


Fig. 3. Styrene-PhSCl adducts (60 Mc, in CCl_4).

Table 16. The Isomer Distribution of the Adducts.

Ar	R	bp. (°C/mm)	Isomer ratio	
			after distillation	before
	CH_3	112/ 8	65/35	98/ 2
〃	C_2H_5	137/14	69/31	
〃	n-C_4H_9	125/ 3	70/30	
〃		155/ 3	69/31	
〃	CH_3O- 	180/ 3	66/34	90/10
〃	CH_3- 	182/14	65/35	87/13
〃	Cl- 	186/14	67/33	
〃	NO_2- 	(155°, 30′)[a] mp 68～72°C	80/20	
〃	NO_2-  -NO_2	(155°, 60′)[a] mp 144～145°C	100/ 0	100/ 0
CH_3- 	CH_3	145/25	72/28	97/ 3
Cl- 	CH_3	135/ 6	65/35	97/ 3
CH_2=$CHCOOCH_3$ + CH_3SCl		116/38	50/50	
CH_2=$CHCN$ + CH_3SCl		109/20 (119/28)[b]	50/50 (35/65)[b]	50/50

a), Heated at the temperature stated.
b), The result obtained from the reaction mixture of DMSO, chloromethyl methyl sulfide.[45]

Characterization of the products was carried out utilizing NMR spectroscopy and chemical techniques (Table 15 and 16). NMR spectra of the methylene-

methine region of two isomers, **42** and **43**, were complex due to ABX and ABC systems of each isomers and dependent upon solvents and sulfenyl chlorides (Fig. 1, 2 and 3).

The rate of isomerization of **42 a** (Ar=Ph, R=CH_3, mp. 25-26°C) was analysed by NMR and solvolysis (Table 17).

Table 17. Rate of Isomerization.

$$\mathbf{42\,a} \underset{}{\overset{k}{\rightleftarrows}} \mathbf{43\,a}$$

Reaction condition	Temperature (°C)	k (sec^{-1})
10% CCl_4 soln.	23	3.9×10^{-8} (N)
10% (80% CCl_4 + 20% CD_3COOD) soln.	23	3.3×10^{-6} (N)
10% CD_3COOD soln.	23	3.5×10^{-5} (N)
10% HCOOH soln.	23	10^{-4} (N, S)
No solvent	30.5	3×10^{-6} (S)
No solvent	0	no isomerization for 8 months (N)

N; NMR, S; Solvolysis

The equilibrium mixture gave only the substitution product of chlorine on Markownikoff adduct *via* episulfonium ion when treated with silver nitrate in methanol, potassium acetate and dilute alkoxide solution *etc.* On the other hand, both isomers gave elimination products in the reaction with concentrated alkoxide solution; especially the anti-Markownikoff adducts underwent very facile elimination reaction to give α-substituted styrenes. These elimination reactions do not seem to proceed *via* episulfonium ion but undergo direct E2 reaction (Table 18).

$$\mathbf{42\,a}\text{ and }\mathbf{43\,a} \longrightarrow \underset{\mathbf{(44)}}{\mathrm{Ph{-}CH(OCH_3){-}CH_2{-}SCH_3}} + \underset{\mathbf{(45)}}{\mathrm{Ph{-}C(SCH_3){=}CH_2}} + \underset{\mathbf{(46)}}{\mathrm{Ph{-}CH{=}CH{-}SCH_3}}$$

Table 18. Solvolysis of the Equilibrium Mixture.

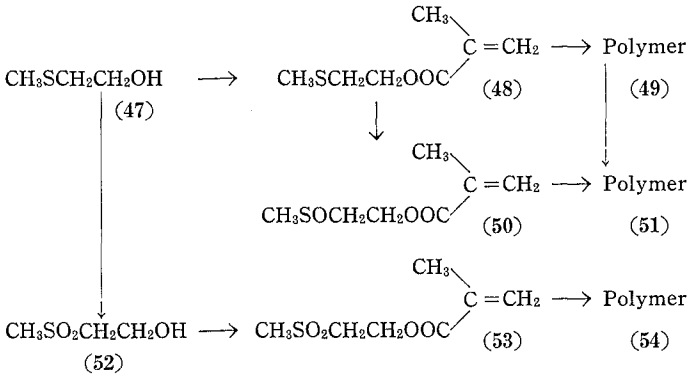
Reaction condition		Ratio of the products		
		44	45	46
In methanol	15% Na	67	33	trace
	10% Na	70	30	trace
	2.5% Na	78	22	0
	1% Na	92	8	0
	silver nitrate	100	0	0
In ethanol	8% Na	51[a]	34	15
In *t*-butanol	5% K		22	78

a) 1-Ethoxy-2-methylthio-1-phenylethane.

α, β-Substituted phenylethanes and substituted styrenes can be easily synthesized by the application of the above-mentioned substitution and elimination reactions.

XI. Syntheses of Poly-[(2-methylsulfinylethyl) methacrylate] and Poly-[(2-methylfulfonylethyl) methacrylate][48]

Only a few examples of water-soluble methacrylate has been reported, although a large number of methacrylate polymers has been prepared. We now wish to report the syntheses of some new monomers of methacrylate and their polymerization. The polymers obtained are very soluble in water and show surface activity in water. The preparative pathways are shown below.



β-Methylthioethyl methacrylate [bp. 113–114°C/33; IR, νCO 1715 cm^{-1} νC=C 1635 cm^{-1}, πC–H 810 cm^{-1}] was prepared by esterification of β-methylthioethanol[49] with methacrylic acid chloride in the presence of pyridine according to an analogous procedure described in literature.[50] The polymerization of 48 was carried out at 70°C initiated by ABIN to white powdered polymer (**49**); softening point 155–180°C, $[\eta]=1.08\ dl\cdot g^{-1}$, soluble in acetone, benzene, dioxane and ethyl acetate.

The polymer **49** ($[\eta]=0.33\ dl\cdot g^{-1}$) was oxidized by hydrogen peroxide in acetone to poly-[(2-methylsulfinylethyl) methacrylate] (**51**); softening point 155–160°C, $[\eta]=0.24\ dl\cdot g^{-1}$, soluble in water and methanol. The aqueous solution of the polymer **51** showed strong effect of nonionic surfactant. Another way of preparation of the polymer **51** was the synthesis of 2-methylsulfinylethyl methacrylate (**50**, liquid) obtained by the oxidation of 48 with hydrogen peroxide, followed by the polymerization of **50**. Elemental analysis and IR spectra of the both polymers were essentially same.

The oxidation of 47 with hydrogen peroxide gave 2-methylsulfonylethyl alcohol (**52**) and the treatment of **52** with methacrylic acid chloride in the presence of pyridine afforded 2-methylsulfonylethyl methacrylate (**53**) bp. 175–185°C (bath)/8; IR, νC=O 1720 cm^{-1}, νC=C 1635 cm^{-1}, νSO_2 1290 and 1120 cm^{-1}. The polymerization of **53** initiated by ABIN gave white polymer (**54**); softening point 170–190°C, $[\eta]=0.3\ dl\cdot g^{-1}$, soluble in acetone and water.

The polymers reported here showed properties of usual methacrylate resins, while unusual solubility of the polymers in water would be of interest to commercial availability.

XII. The Preparation of Some Surfactants Containing Sulfoxide and/or Amine oxide[51]

Surface-active compounds are all made up of molecules containing hydro-

philic and hydrophobic groups. Three types of surfactant are known; cation-active, anion-active and nonionic surfactants (and ampholytic surfactant).

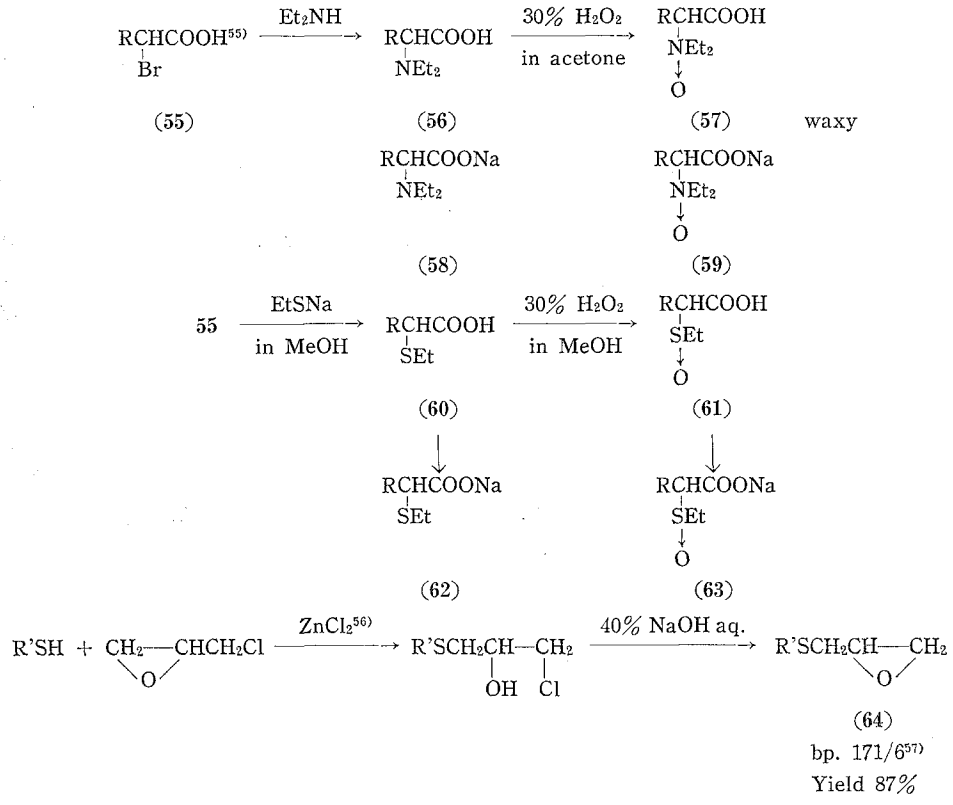
Although the unusual surface activity of detergents which contain sulfoxide or amine oxide as nonionic hydrophilic groups has long been known, only preliminary reports or patents have appeared to the syntheses and behaviors of the surfactants.[52~54] The unique behavior of methylsulfinyl-ethyl methacrylate polymer[48] has prompted us to investigate the surface properties of these materials. Preparative procedures, isolation and purification of these materials are reported briefly and surface tention in aqueous media is described.

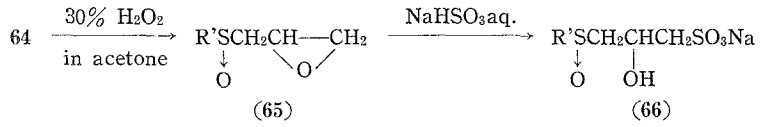
Preparative procedures and formula of new surfactants are shown in Chart 1 and Table 19. For convenience, following abbreviations are used to the structural formula of the surfactants.

$$R = n\text{-}C_{10}H_{21}, \qquad R' = n\text{-}C_{12}H_{25}$$

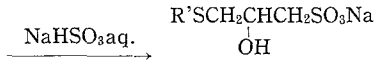
Purification of some compounds which are shown as "waxy" in Chart 1 was difficult and analytically pure materials could not isolated. Surface tension measurements were made on Du Noüy surface and interfacial tentiometer (Shimazu Seisakusho LTD) at 20°C. The results obtained are shown in Table 20. At left side of the upper part of Table 20, compounds having sulfoxide group are arranged and the corresponding amine oxides are shown at the right side.

Chart 1. Preparative procedure.

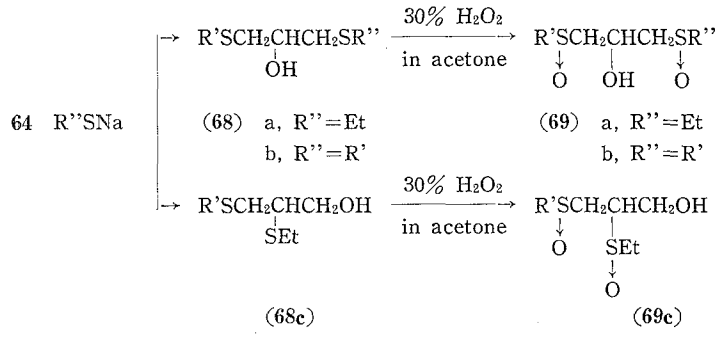




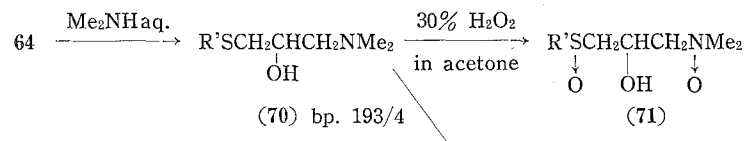
(65) (66)



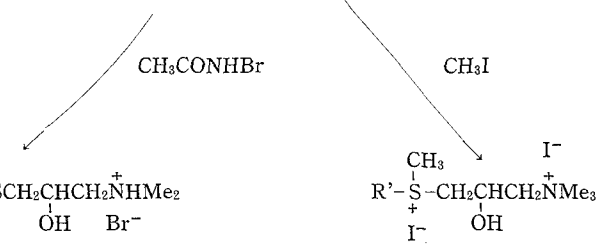
(67)



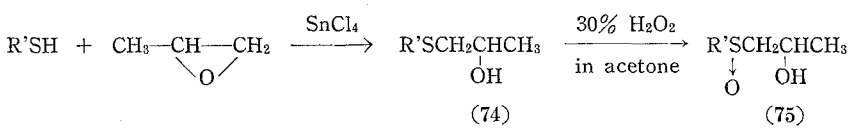
(68c) (69c)



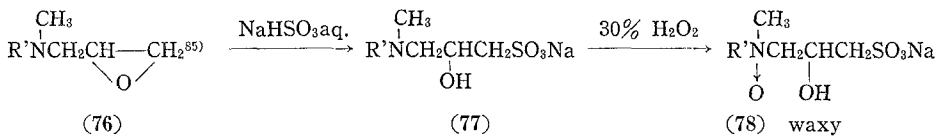
(70) bp. 193/4 (71)



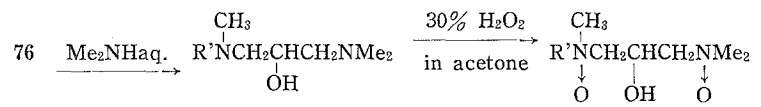
(73) (72)



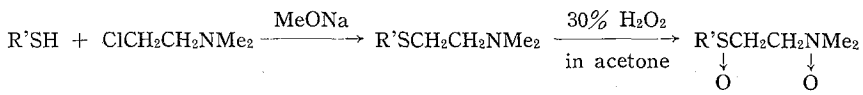
(74) (75)



(76) (77) (78) waxy



(79) bp. 205/18 (80) waxy



(81) (82)

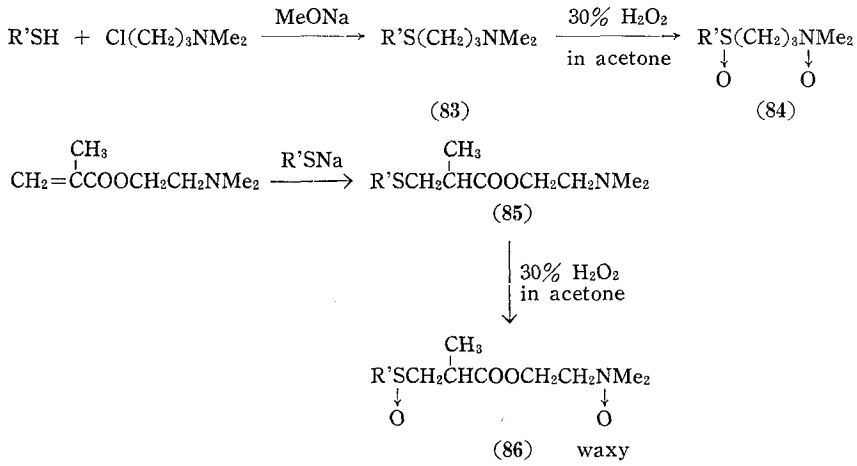


Table 19

Compound	Mp. (°C) or Bp. (°C/mm)	Recrystn. solvent	Yield (%)
56	56– 58	Acetone	78
62	38– 40 (215/19)	Methanol	70
63	95– 97	Methanol	46
65	63– 64	Petroleum ether	93
66		aq. Ethanol	71
68a+68b	220–222/4		78
69a	112–115	Acetone	38
69c	87– 89	Acetone	45
68b	41– 44	Acetone	79
69b	112–117		81
7b	108–112		66
72	105–107	Ethanol	69
73	115–118	Ethanol	23
75	80– 83	Acetone	78
80	Monopicrate 110–112	Ethanol	
81	170–172/4		81
82[a)]	74– 77	Acetone	100
83	177–179/4		88
84[a)]	119–120	Acetone	100
85	216–218/4		76

a) Hygroscopic compound.

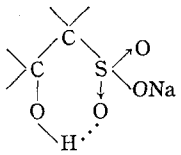
Some of the new surfactants reported here **60, 61, 65, 66, 67, 69 a, b, c, 75, 77, 78** are insoluble or hardly soluble in water and these results suggest that contribution of sulfoxide group as a hydrophilic group to solubility in water is small. It is surprising that such a compound having sodium sulfonate group as **66, 77** and **78** has also a limited solubility in water.

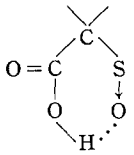
Low solubility of these compounds may be explained by intramolecular hydrogen bonding[59] as shown below.

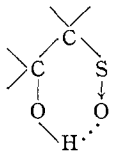
Table 20. Surface Tension.

Compound	Surface tension		Compound	Surface tension	
	1% soln.	0.5% soln.		1% soln.	0.5% soln.
67	30.6[a]	31.1[b]	**23**	32.2[a]	42.5[b]
66	37.4[c]		**24**		
60	[d]	[d]	**2**	34.3	34.2
61	31.7[c]		**3**	29.0	28.8
62	27.3	34.3	**4**	32.3	33.6
63	36.1	31.5	**5**	29.3	27.2
65	25.4[c]				
75	27.7[c]				
69a	41.2[c]		**26**	30.0	29.4
69c	41.2[c]				
71	29.3	29.7			
84	37.6	37.8			
82	26.1	25.8			
86	28.1	26.3			
73	38.9	34.4			
72	40.3	40.3			

a) 0.1% Soln.
b) 0.05% Soln.
c) Saturated soln. (the concentrations are below 0.1%, solubility of these compounds in water are very small).
d) Measurements was impossible because the compound is scarcely soluble in water.







Hydrogen bonding was substantiated by IR(streching of OH was shifted to about 3200 cm^{-1}).

On the other hand, the corresponding amine oxide surfactants are easily soluble in water and amine oxide group is superior to sulfoxide group as nonionic hydrophilic groups.

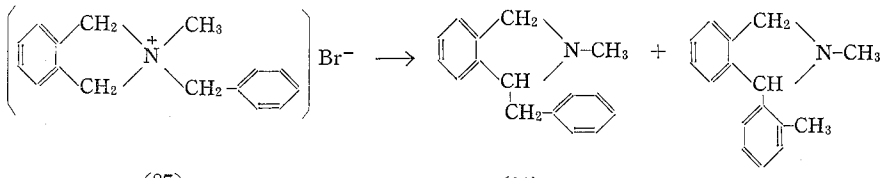
While some of the new surfactants show good surface tention lowering in aqueous media, comparison of surface activity with these surfactants may be difficult without detergent and wetting properties and cmc of the surfactants.

XIII. The Sommelet Rearrangement of Sulfonium Salts[60]

Details of the reaction conditions of the preparation of sulfur-ylides are still not fully settled, although recent publication have covered their preparation. We are anxious to determine how reaction conditions would effect the distribution of the products.

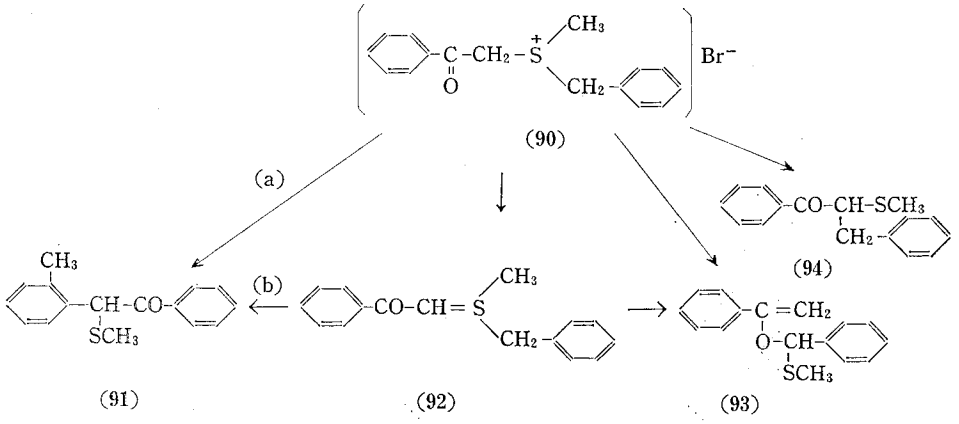
The Stevens and the Sommelet rearrangements of ammonium salts have been extensively studied. Wittig and Streib[61] found decreasing yields of Sommelet

rearrangement product (89) and increasing yields of Stevens product (88) as the temperature increased, when the ammonium salt (87) was treated with bases. An interpretation is given for the temperature dependence of the product distribution.[62]



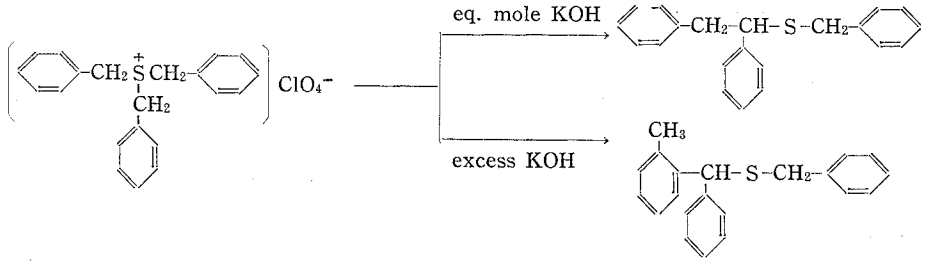
(87) (88) (89)

Similar rearrangements have been observed with sulfonium salts. Ratts and Yao[63] investigated the rearrangement of the sulfonium salt (90) as a function of reaction conditions and base concentration. Sommelet rearrangement of the sulfonium salt 90 has not been shown in literature.



(90) (91) (92) (93) (94)

The amount of base is one of the factors controlling whether the Stevens or the Sommelet rearrangement occurs in the reaction of tribenzylsulfonium salt.[64]



The base concentration dependence of the product distribution, however, has not been widely studied, therefore, we reexamined the reaction of 87[61] and 90[63].

We found that in general these product distributions are dependent on concentration of base, however, independent on equivalent amounts of base. The results obtained are shown in Table 21 and 22 (the ratio of the products was

determined by nmr analysis).

Table 21. The ratio of the products, 88 and 89.

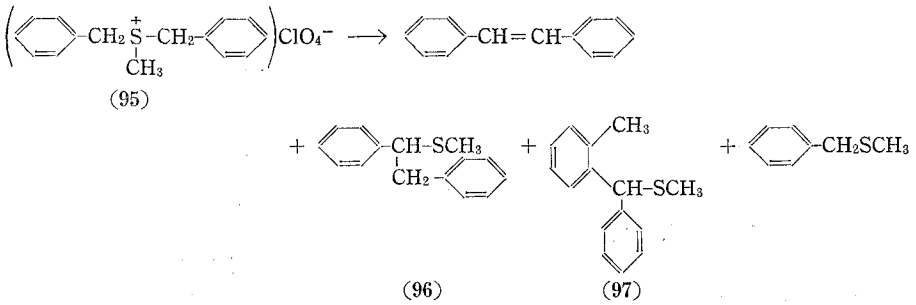
Reaction condition	88	89
3% Na in ethanol at 80°C	90	10
10% Na in ethanol at 80°C	50	50
10% phenyl lithium in ether at 25–35°C	15	85

Table 22. Yields (%) of the products, 91 and 93.

Reaction condition	91	93
5% Na in methanol	3	78
10% Na 〃	48	32
15% Na 〃	69	trace

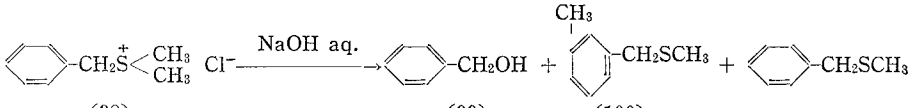
It can be seen from Table 21 and 22 that base concentration is also one of the important factors for the products distribution. The salt **90** gave pure sulfide **91** (bp 178°/6; sulfone, mp 137–139°C), when **90** was treated with 35% sodium methoxide (=15% Na) in methanol at 60–65°C for 2 hr (condition A). The ylide **92** also gave **91** (30% yield) under the condition A.

The ratio of the Sommelet (**97**: bp 148–149°C/6 mm; sulfone, mp 94–96°C) to the Stevens (**96**: bp 185°C/27 mm; sulfone, mp 117–119°C) rearrangement product was increased as the concentration of base was raised, when the perchlorate (**95**) was treated with sodium methoxide in methanol [Sommelet: Stevens; 95 : 5 (15% Na), 45 : 55 (1% Na)].



(95) (96) (97)

Aqueous solution of benzyldimethylsulfonium chloride (**98**) gave increasing yields of the Sommelet rearrangement product[65] and decreasing yields of the benzyl alcohol[66] as the concentration of base was raised, when **98** was treated with sodium hydroxide (Table 23).



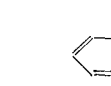
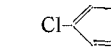
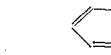
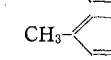
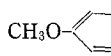
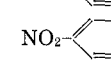
(98) (99) (100)

Table 23

Reaction condition (conc. of 98; mole/l)	Yield (%) 99	100
0.15	95	trace
2.5	3	35
4.5	trace	87

In the similar manner, sulfonium perchlorates gave substitution products and Sommelet rearrangement products, when perchlorates were treated with sodium methoxide. Some examples of the reactions are shown in Table 24.

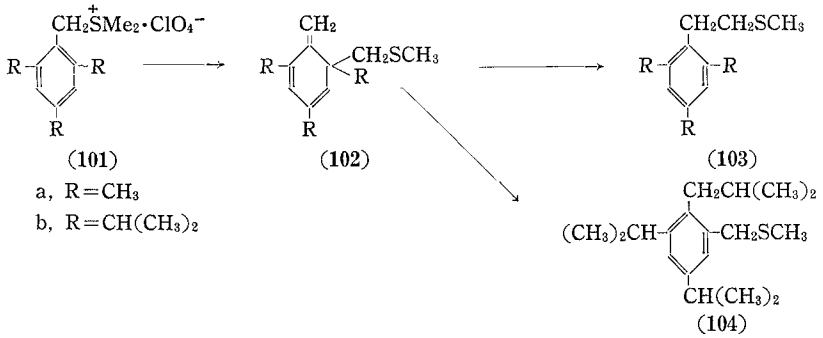
Table 24. Yields (%) of products.

$(R\text{-}SMe_2)X$	$X=ClO_4$[a]		$X=Cl$[b]		
R-	$ROCH_3$	Rearr.[c]	ROH	R_2O	Rearr.[c]
	11	85	13	0	64
	29	56	4	7	70
	60	40	3	50	35
	82	15	11	36	33
	84	3	—	—	—
	only dinitrostilbene was isolated[67]				

[a] Perchlorate was treated under the condition A.
[b] 2.5 M sulfonium chloride aqueous solution (0.1 mole) was treated with 30% sodium hydroxide aqueous solution (0.2 mole).
[c] Sommelet rearrangement product.

Pure Sommelet rearrangement products can be isolated from the reaction of **98** or **95** and potassium *t*-butoxide in *t*-butanol (or phenyl lithium in ether), while benzyldimethylphenacylammonium bromide gave only Stevens product by treatment with any bases.

When both ortho positions are occupied, sulfonium salts gave exo-methylenecyclohexadiene derivatives (**102**) (90-95% yield) by the reaction of potassium *t*-butoxide in *t*-butanol. The cyclohexadienes undergo thermal isomerization to aromatic products as ammonium salts.[68] In the case of **102 b**, main product (80% yield) was **104** (bp 135-137°C/3; sulfone, mp 105-107°C), while **102 a** gave **103 a** (bp 160-165°C/26; sulfone, mp 154-156°C).



XIV. The Reaction of Carbonyl-Stabilized Sulfur Ylides with Nitrile Imines; A Facile Preparation of Pyrazoles[69]

Recent publications concerned with resonance-stabilized sulfonium ylides have

covered their preparation, but relatively few of their chemical reactions have been described.

1, 3-Dipoles are useful starting materials for the synthesis of heterocycles. In a recent note,[70] the result of the reaction between nitrile imine and dimethyloxosulfonium methylide was reported. The latter ylide was shown to cause consecutive transfer of two methylene groups to the former, giving rise to a pyrazoline. The reaction of phosphorus ylides with nitrile oxides gave interesting products.[71]

We investigated the reaction of carbonyl-stabilized sulfur ylides with nitrile imines by mixing a cold benzene solution of sulfur ylides with N-(α-chlorobenzylidene)-N′-phenylhydrazine, a precursor of nitrile imine. The sulfur ylides acted as bases to generate the nitrile imine and the sulfonium chloride precipitated quantitatively.

Chart 2.

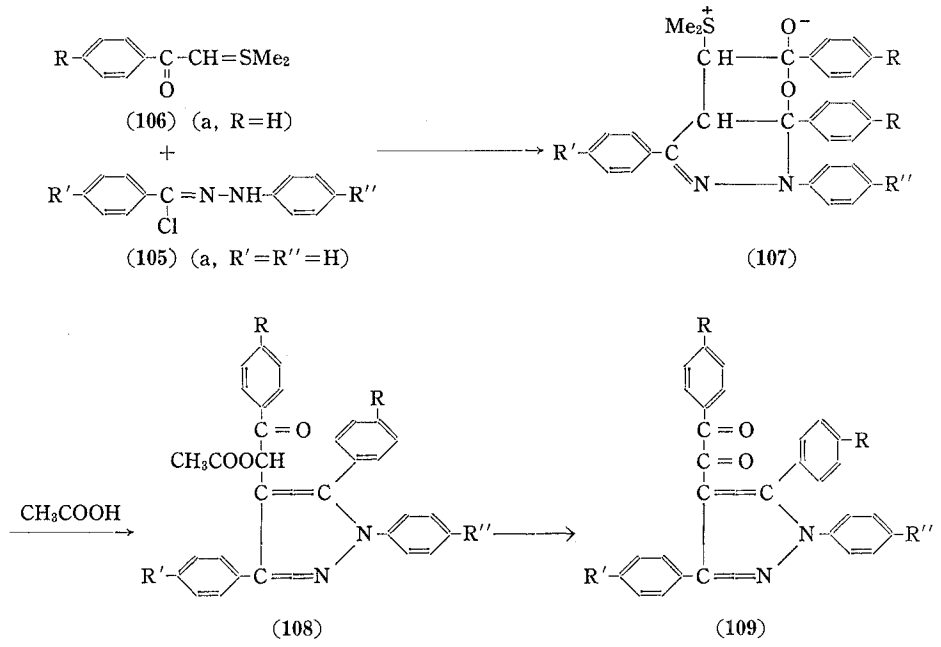


Table 25. Melting Point (°C) of the Products.

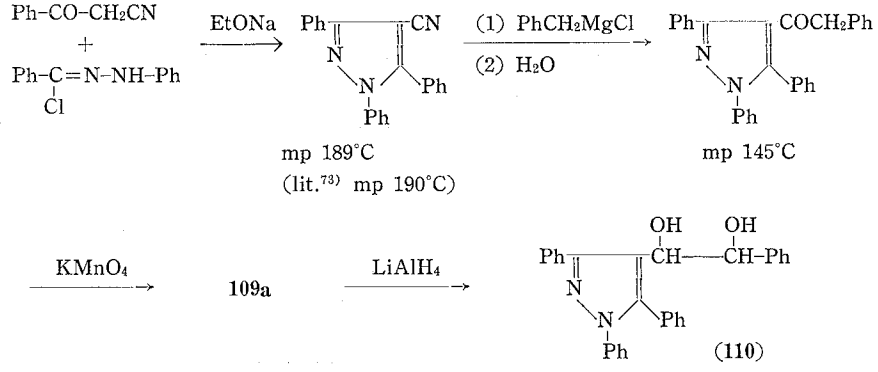
	R	R′	R″	107	108	109
a	H	H	H	158–159	137–139	155–157
b	H	CH_3	H	157–159	152–153	123–124
c	CH_3	H	H	147–148	170–172	155–157
d	H	H	NO_2	135–136	152–154	144–145
e	Br	H	H	183–184	176–177	164–165
f	H	H	Cl	163–164	151–153	136–137
g	Cl	H	H	179–180	165–167	167–168

The results are summarized in Chart 2 and Table 25 (satisfactory elemental analyses and spectral data were obtained).

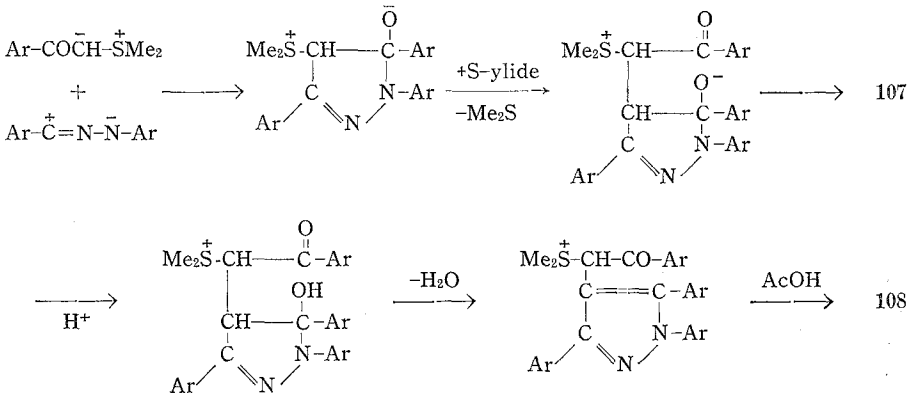
The reaction between **105 a** and **106 a** is described as the representative. The precipitate from the reaction mixture was washed with warm water to leave a pale pink almost pure product (**107 a**). Recrystallization of the product from ethylenedichloride gave an analytical sample; IR (nujol), no C=O, N-H and OH streching; anal., $C_{31}H_{28}N_2O_2S$; 95% yield based on **105 a**. Definitely clear NMR spectra of **107 a** were not available as solubility of **107 a** in common solvents was very small and **107 a** was not stable at high temperatures. **107 a** is soluble in acetic acid developing red color which fades away within a day at room temperature. A product (**108 a**, quantitative yield) was isolated from this colorless solution and dimethyl sulfide (as mercuric chloride complex, 70% yield) was also obtained from the volatile portion of the solution. These reactions were traced by NMR in perdeuteroacetic acid. NMR spectrum of the red solution showed, COOH at τ-1.22 (singlet, 2 H), ArH at τ 2.2-2.9 (multiplet, 2 OH), SCH_3 at τ 6.91 and τ 7.12 (two 3 H singlets). Two singlets at τ 6.91 and τ 7.12 disappeared gradually and new singlet at τ 7.97 (CH_3SCH_3) appeared. The rate of appearance of the new singlet was first order (k is about 5×10^{-5} sec^{-1} at 24°C). Recrystallization of **108 a** from ethanol gave an analytical sample; IR (nujol), νC=O 1740, 1705 cm^{-1}; NMR ($CDCl_3$), ArH at τ 2.2-3.0 (multiplet, 2 OH), -CH< at τ 3.05 (singlet, 1 H), $COCH_3$ at τ 7.71 (singlet, 3 H); anal., $C_{31}H_{24}N_2O_3$ (MW, calcd.: 472.5, found: 456). Hydrolysis of **108 a** in ethanolic potassium hydroxide solution gave a pale yellow product (**109 a**, 90% yield); IR (nujol), νC=O 1685, 1650 cm^{-1}; NMR ($CDCl_3$), ArH at τ 2.10-2.90 (multiplet); anal., $C_{29}H_{20}N_2O_2$. **109 a** is stable in concentrated sulfuric acid and to permanganate oxidation, hydrogen peroxide oxidation in acetic acid (the reaction conditions of oxidation of benzils[72]). Lithium aluminum hydride reduction of **109 a** gave a glycol (**110**); mp 157°C; NMR ($CDCl_3$), ArH at τ 1.45-2.2, 2.4-2.9 (multiplet, 20 H), -CH< at τ 5.23 and τ 5.45 (two doublets, 2 H, J_{H-H}=8 cps), OH at τ 8.11 (singlet, 2 H); anal., $C_{29}H_{24}N_2O_2$.

The structure of **109 a** was shown to be benzoyl [1, 3, 5-triphenylpyrazolyl-(4)] ketone by its failure to depress the melting point of an authentic specimen prepared as described in Chart 3.

Chart 3.



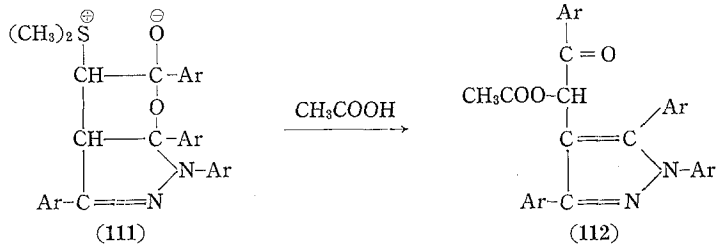
The structural assignment of **108** seems reasonable from the results mentioned above and facile oxidation of benzoins.[74] The structure of **107** is not yet substantiated, but some tentative conclusions about the mechanism of these reactions can be drawn as described below.



These mechanisms suggest the resemblance to the reaction of the sodium derivatives of active methylene compounds with α-halohydrazones, an economical and practical method of pyrazole synthesis[75] (see Chart 2).

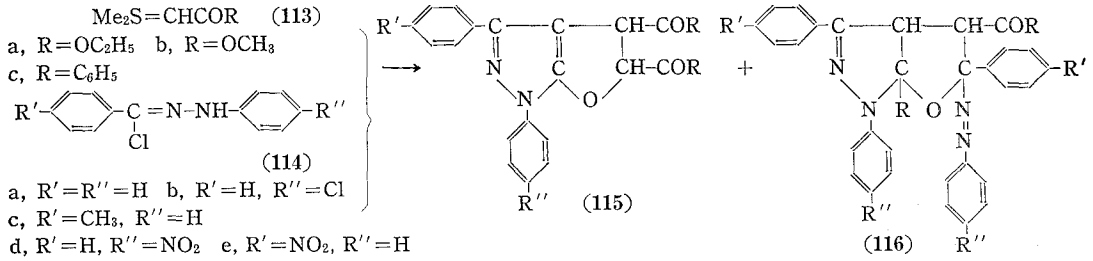
XV. The Reaction of Carboalkoxymethylenesulfuranes with Nitrile Imines[76]

In previous paper,[69] we reported the reaction of phenacyl sulfonium ylides with nitrile imines, yielding betaine **111** in excellent yields. The betaine can be converted conveniently and in good yields to pyrazole **112**.



In continuing our study of ylides, we have investigated the reaction of nitrile imines with alkyl dimethylsulfuranylidene acetate, one of the carbonyl-stabilized

Chart 4.



sulfur ylides. The results reported here conclusively demonstrate that the reaction products are dependent upon the structure of the ylides and the nitrile imines.

Reaction of nitrile imine precursor **114 a** with excess of ylide **113 a** in benzene at room temperature afforded a 62% yield of diester **115 a** and a small amounts of yellow-brown azo compound **116 a**, while equimolar mixture of **113 a** and **114 a** gave a 36% yield of **116 a**.

The results obtained are shown in Chart 4 and Table 26.

Table 26. Melting Point (°C) and Yield (%) of the Products.

115

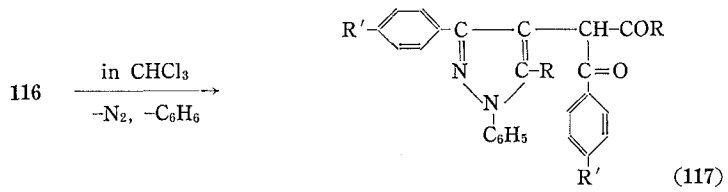
	R	R′	R″	MP.	yield
a,	OC_2H_5	H	H	121–122	62
b,	OCH_3	H	H	99–101	53
c,	OC_2H_5	H	Cl	170–171	54
d,	OCH_3	H	Cl	132–133	13

116

	R	R′	R″	MP. (dec.)	yield
a,	OC_2H_5	H	H	135–136	36
b,	OCH_3	H	H	138–139	74
c,	OCH_3	CH_3	H	141–142	56
d,	C_6H_5	H	H	152–154	5

The structural assignment of **115 a** was substantiated by elemental analysis; molecular weight; IR (all in Nujol), νC=O 1703, 1728, and 1744 cm^{-1}; NMR (all at 60 Mc in τ units) (in $CDCl_3$), 2.0–3.0 (m. 10, aromatic H), 5.72 (q. 2, methylene H), 6.41 (m. centered at, 2, methylene H), 5.72 and 6.77 (two d. 2, methine H, J=8.5 cps), 8.71 and 9.07 (two t. 6, methyl H) and alkaline hydrolysis to dibasic acid (mp. 210°C).

The tentative structure of **116 c** was based on elemental analysis; molecular weight; IR, νC=O 1718 and 1735 cm^{-1}; and NMR (in C_6D_6), 2.0–3.4 (m. 18, aromatic H), 5.06 and 5.92 (two d. 2, methine H), 6.95 and 7.21 (two s. 6, methoxy H), 7.86 and 7.99 (two s. 6, methyl H). Acid catalyzed thermal decomposition in ethanol or facile decomposition of **116 c** in chloroform at room temperature gave nitrogen gas, benzene and pale yellow crystals; mp. 125–128°C; elemental analysis, $C_{28}H_{26}N_2O_4$; IR, νC=O 1682 and 1740 cm^{-1}; NMR (in $CDCl_3$), 2.0–3.3 (m. 13, aromatic H), 4.58 (s. 1, methine H), 6.31 and 6.48 (two s. 6, methoxy H), 7.58 and 7.71 (two s. 6, methyl H). The data mentioned above are consistent with the assignment of **117 b** as the decomposition product.



(117)

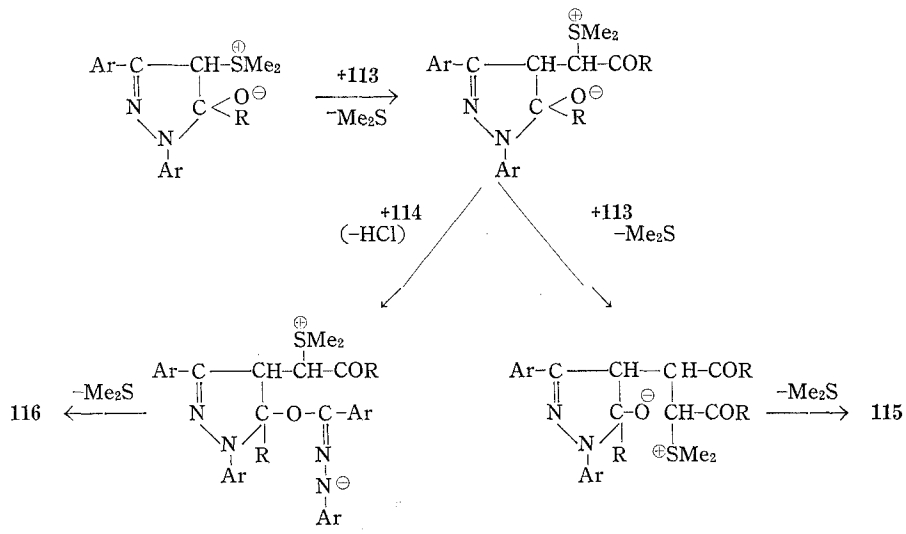
a, R=OCH_3, R′=H, mp. 148–151°C
b, R=OCH_3, R′=CH_3, mp. 125–128°C
c, R=C_6H_5, R′=H, mp. 133–136°C

Remarkable shift upfield of the alkoxy methyl band of azo compounds **116** contrasts sharply with the usual positions for these groups. The NMR spectrum

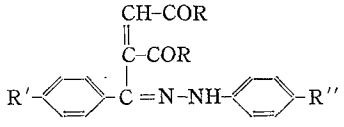
(in C_6D_6) of the ethoxy methyl bands of **116 a** shows two triplets at 9.35 and 9.49.

Some tentative conclusions about the mechanism of these reactions can be drawn as in Chart 5. The sharp difference in reactivity between **113**, R=O-alkyl and **113**, R=aryl is unexpected[86] and only one common product **116** was isolated from the reaction mixtures.

Chart 5.



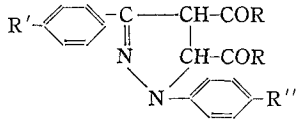
On the other hand, treatment of **114 d** with **113 a** in benzene at 25°C for 24 hours gave **120 a** and **121 a** in yield of 18% and 22%, respectively. The structure of **121 a** was established by its identity with the adduct of **114 d** and diethyl fumarate[77] and the mechanism of the formation of **121** may be analogous to the reaction of nitrile imines with dimethyloxosulfonium methylide.[70]



(120)

a, R=OC_2H_5, R'=H, R''=NO_2
mp. 178–180°C

b, R=OCH_3, R'=H, R''=NO_2
mp. 201–202°C



(121)

a, R=OC_2H_5, R'=H R''=NO_2
mp. 115–117°C

b, R=OCH_3, R'=H R''=NO_2
mp. 166–168°C

c, R=OC_2H_5, R'=NO_2, R''=H
mp. 107–108°C

Recrystallization of **120 a** from ethanol gave pale yellow crystals; IR, significant absorption at 3270 cm^{-1} (m), 1730 cm^{-1} (s), 1720 cm^{-1} (s), 1623 cm^{-1} (m); NMR (in $CDCl_3$), 1.6–3.1 (m. 9, aromatic H), 4.46 (s. 1, olefinic H), 5.46 and 5.85 (two q. 4, methylene H), 8.50 and 8.73 (two t. 6. methyl H).

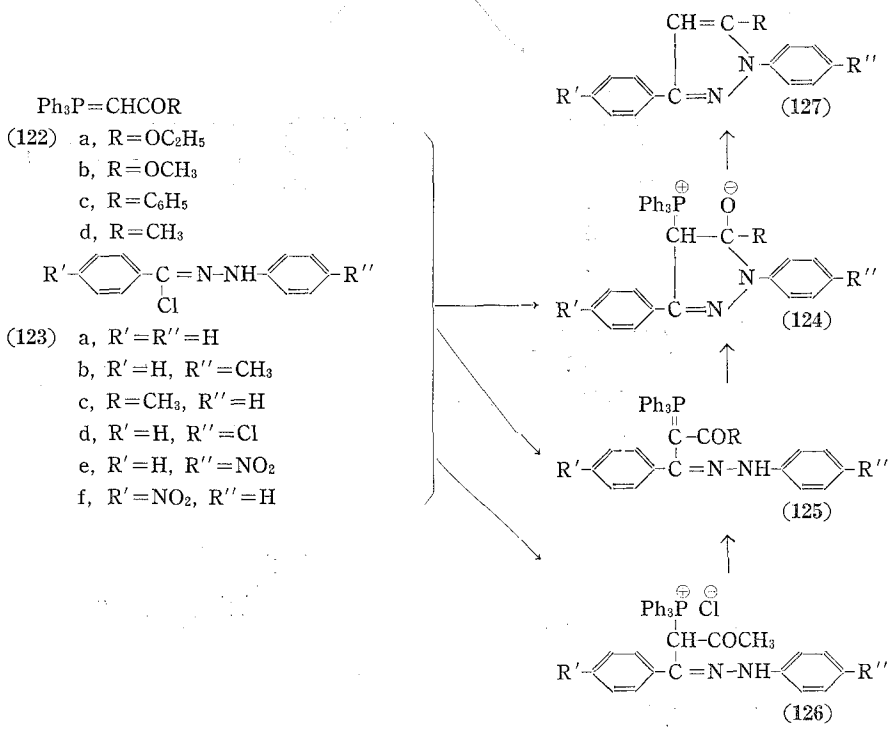
The formation of **120** and **121** may be ascribed to the electron-withdrawing

effect (stabilization of nitrogen anion of the nitrile imine) of nitro group of **114d**. The reaction of **114e** with **113a** gave **121c** in 81% yield.

XVI. The Reaction of Carbonyl-Stabilized Phosphorous Ylides with Nitrile Imines; A new Synthetic Method of Pyrazoles[78]

From a study of the recent publications[69,70] concerned with the reaction of 1, 3-dipoles with sulfur ylides, we were particularly anxious to determine how carbonyl-stabilized phosphorous ylides would react with nitrile imines, although this reaction would be expected to parallel the reaction of phosphorous ylides with organic azides.[79] We wish to report at this time the results of our work which clearly show that the reaction products are dependent on the electron-donating character of carbonyl group of the ylides (**122**) and independent on α-chloroarylhydrazones (**123**), a precursor of nitrile imines. The results obtained are summarized in Chart 6, Table 27 and Table 28.

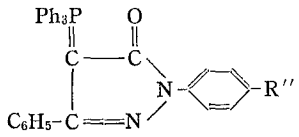
Chart 6.



The ylide **122a** reacted with nitrile imine precursor **123a** in the presence of triethylamine at ambient temperature for 24 hours to furnish triethylamine hydrochloride and colorless crystals quantitatively, mp. 152-153°C; elemental analysis and molecular weight, $C_{35}H_{31}N_2O_2P$; UV, λ_{max} 303 and 345 mμ; IR (all in Nujol), no significant absorption at 3100-3600 cm^{-1}, νC=O, 1624 cm^{-1}; NMR (all at 60 Mc in $CDCl_3$ in τ unit), 1.35 (s. 1, acidic H), 2.2-3.3 (m. 25, aromatic H), 6.00 (q. 2, methylene H, J=7 cps), 8.7-9.35 (broad, 3, methyl H).

Addition of trace amounts of acetic acid produced line sharpening (triplet)

of the ethoxy methyl band of the NMR spectrum of the product, while other resonances in the spectrum remained essentially unchanged. Pyrolysis of the product yielded quantitatively pyrazole **127 a**[77] and triphenylphosphine oxide. A remarkable solvolysis of the product (or **125 b**) in acetic acid at room temperature was observed to furnish new ylide **128 a** quantitatively.



(128)

a, R″=H, mp. 235–237°C; IR, νC=O 1626 cm^{-1}; NMR, 1.85–3.3 (m. aromatic H).

b, R″=CH_3, mp. 281–283°C; IR, νC=O 1624 cm^{-1}; NMR, 1.8–3.2 (m. 24, aromatic H), 7.69 (s. 3, methyl H).

c, R″=Cl, mp. 284–286°C; νC=O 1625 cm^{-1}; NMR, 1.7–3.3 (m. aromatic H).

The data mentioned above show the reaction product to be **125 a** or a mixture of **125 a** and betaine form (**124 a**) of **125 a.** Geminal P-H coupling in the spectrum could not be observable but this result not necessarily means that the dominant isomer is **125 a.**[80]

Table 27. Melting Point (°C) of the Products.

125 (and/or 124)

	R	R′	R″	MP. (dec.)
a	OC_2H_5	H	H	152–153
b	OCH_3	H	H	155–156
c	OC_2H_5	H	CH_3	151–153
d	OC_2H_5	H	Cl	128–129
e	OCH_3	H	Cl	132–134
f	OC_2H_5	H	NO_2	124–125
g	OCH_3	H	NO_2	111–112
h	OC_2H_5	NO_2	H	137–138
i	OC_2H_5	CH_3	H	149–151
j	CH_3	H	H	193–194
k	CH_3	CH_3	H	130–133

127

	R	R′	R″	MP. (dec.)
a	OC_2H_5	H	H	67– 68
b	OC_2H_5	H	Cl	87– 88
c	OC_2H_5	H	NO_2	163–164
d	OCH_3	H	NO_2	187–189
e	OCH_3	H	Cl	68– 70
f	OC_2H_5	CH_3	H	62– 63
g	OC_2H_5	NO_2	H	125–126
h	CH_3	H	H	208/28 (bp)
i	C_6H_5	H	H	137–139

The reaction of **122 a** with **123 d** (or **123 e**) also gave **125 e** (or **125 f**) quantitatively within 3 hrs at 10°C, while longer reaction time (one day) at room temperature gave directly pyrazole **127 b** (or **127 d**) and triphenylphosphine oxide in high yield. Electron-withdrawing chloro (or nitro) substituent may destabilize the intermediate **124** and facile Wittig-type elimination of the phosphine oxide would give pyrazole. 1, 3, 5-Triphenylpyrazole **127 i** (24% yield) was also isolated by repeated recrystallization of the reaction mixture of **122 c** and **123 a.**

When the ylides are strongly basic as in **122 d,** the reaction with the nitrile imine precursors took a different and anomalous course and let to phosphonium salt **126** in spite of the presence of excess triethylamine or the ylide. The acetonyl ylide **122 d** required only 4 hours for complete conversion to phosphonium salt **126 b** in benzene at room temperature.

Table 28. Melting Point (dec. °C) of Phosphonium Salt **126**.

a	$R=CH_3$,	$R'=H$,	$R''=H$	233–234
b	$R=CH_3$,	$R'=H$,	$R''=NO_2$	239–241
c	$R=CH_3$,	$R'=H$,	$R''=CH_3$	245–247

Recrystallization of **126 b** from ethanol gave pale yellow crystals (m. 150–152°C) accompanied by about one mole of ethanol which could be liberated completely at 180°C. The structural assignment of **126 a** was based on elemental analysis; IR, no ν O-H, and ν N-H absorption, ν C=O 1670 cm^{-1} (m); NMR, 1.6–2.8 (m. 25, aromatic H), 5.48 (d. 1, methine H, J=15 cps), 8.03 (s. 3, methyl H); pyrolysis to triphenylphosphine as an isolable product and conversion to **125 j** by 1% sodium hydroxide aqueous solution.

Repeated precipitation of **125 j** from chloroform solution by adding benzene gave pale yellow crystals (70% yield), mp. 193–194°C; elemental analysis, $C_{34}H_{29}N_2OP$; IR, no ν O-H and ν N-H absorption; NMR, 1.8–2.9 (m), 3.29 (s), 6.91 (d, J=25 cps), 7.88 (d, J=2 cps), 8.0–8.4 (broad); 25 : 2/3 : 1/3 : 1 : 2. Addition of trace amounts of acetic acid produced line sharpening (singlet) of the broad methyl band of **125 j**, while other resonances remained unchanged. Equimolar mixture of **125 j** and acetic acid was soluble in water and remarkable solvolysis of the solution was observed to furnish N-benzoylphenylhydrazine (67% yield). Pyrolysis of **125 j** gave 1, 3-diphenyl-5-methylpyrazole **127 h** and triphenylphosphine oxide in high yield and this result is consistent with the mass spectrum of **125 j** which is superimposer of that of the pyrazole and the phosphine oxide.

The data mentioned above suggest the structure of the alkaline treatment product to be **125 j** or a mixture of **125 j** and **124 j**, although stable existence of the betaine form **124** is unusual.

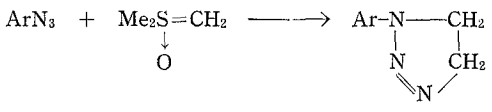
The IR spectrum of **125** (**a**, **e**, **h** and **i**) shows an extremely weak and sharp absorption at about 3240 cm^{-1} which suggests the presence of NH group, while no absorptions between 3100–3600 cm^{-1} could be detected in the other spectra of **125**.

The new reactions reported here are indicative of the reaction spectrum of the ylides and the pyrazole synthesis has extensive utility, although substantial structure of the products is not clear.

XVII. The Reaction of Carbonyl-Stabilized Sulfur Ylides with Azides[81]

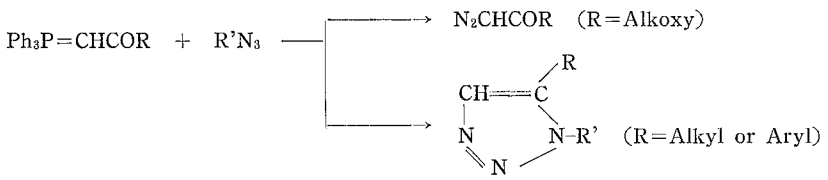
We previously observed[69] that carbonyl-stabilized sulfur ylides react with nitrile imines to give betaines, which afford pyrazole derivatives, in high yield, by subsequent treatment with acetic acid. This reaction sequence appears to offer considerable promise as a synthetic method for heterocyclic compounds.

It is known that the reaction of aryl azide with dimethyloxosulfonium methylide gives aryltriazoline.[70]



The reaction of sulfur ylides with organic azides would be parallel the reac-

tion of phosphorus ylides with the azides.[79]



We now wish to report studies of the reaction of azides with carbonyl-stabilized sulfur ylides and have found that the reaction with arylazides took a different course and led to arylamino dibenzoylethylene (**134**) and no triazoles could be detected (Chart 7, Table 29).

Chart 7. Tentative Reaction Sequence.

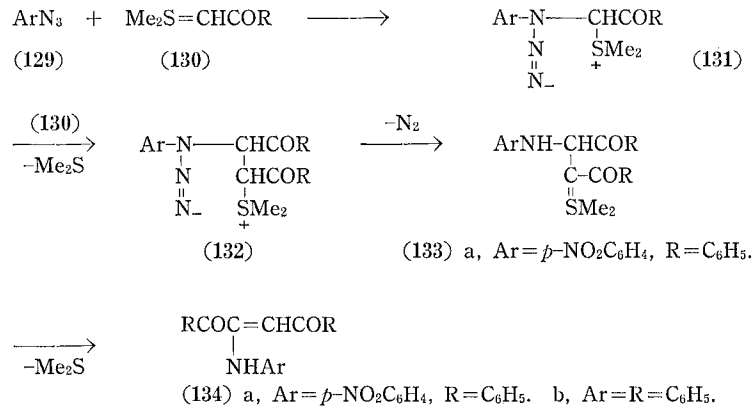
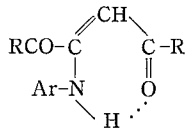


Table 29. Arylamino Dibenzoylethylene.

Ar	R	Yield (%)	Mp. (°C)
C_6H_5	C_6H_5	89	126–128
p-$NO_2C_6H_4$	C_6H_5	60	167–168
p-$CH_3C_6H_4$	C_6H_5	29	153–154.5
C_6H_5	*p*-$CH_3C_6H_4$	100	141.5–142.5
p-$NO_2C_6H_4$	*p*-$CH_3C_6H_4$	99	203.5–204.5
C_6H_5	*p*-BrC_6H_4	100	169–170
p-$NO_2C_6H_4$	*p*-BrC_6H_4	97	221–222

The reaction was carried out by adding *p*-nitrophenyl azide to the solution of dimethyl sulfonium phenacylide in benzene at room temperature. After evolution of nitrogen gas subsided, the precipitate from the reaction mixture was collected and washed with benzene. The precipitate (yield, 40%) was fairly unstable and decomposed slowly to *p*-nitroanilino dibenzoylethylene (**134 a**) and dimethyl sulfide at room temperature. Elemental analysis and IR (in Nujol, definitive absorption of NH at 3350 cm^{-1}) of the precipitate would suggest the structure to be **133 a**, although definitively clear NMR spectra of **133 a** were not available.

From the combined filtrate, **134 a** was isolated in 60% yield. The structural assignment of anilino dibenzoylethylene (**134 b**) was substantiated by elemental analysis; IR (in Nujol), ν C=O 1660 cm^{-1}; NMR (in $CDCl_3$, τ unit), at −2.23 (s, 1, amino H), at 2.1-3.35 (m, 15, aromatic H), at 4.03 (s, 1, olefinic H) and its failure to depress the melting point of an authentic specimen prepared as described in literature.[82] Disappearance of NH absorption and unusual down-field shift in the spectra of **134** suggest strong hydrogen bonding.



In similar experiments as above but using other aryl azides, only anilino dibenzoylethylenes were isolated. No reaction was observed between dimethyl sulfonium phenacylide and alkyl azides even after prolonged heating in benzene.

Azide has several dipolar cannonical forms of a resonance hybrid as follows.

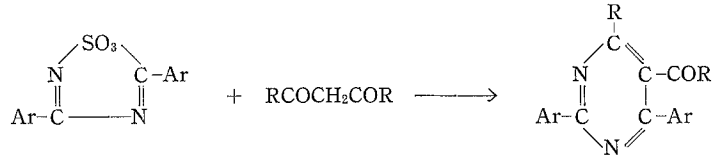
In many cases, nucleophilic attack occurs on azide terminus to give initially a triazo intermediate,[79] while in the reaction of aryl azide with dimethyloxosulfonium methylide nucleophilic attack occurs on anilino nitrogen.[70] Indeed, the initial adduct (**131**) in our work fall within the latter group. Consecutive transfer of two phenacyl groups to the azide gives **132** and this mechanism is also compatible with observed results reported.[69,70] Another possible mechanism of the formation of **134** would be initial formation of dibenzoyltriazoline followed the facile decomposition of the triazoline to **134**.

A possible explanation of the difference of the product between sulfur and phosphorous ylides is that dimethyl sulfide is better leaving group than triphenylphosphine and resonance stabilization of dibenzoylethylene may be larger than that of triazoline.

XVIII. The Reaction of Carbonyl-stabilized Sulfur Ylides with 1, 4-Dipolar Compound; A New Synthetic Method of Pyrimidines[83]

One of the most useful synthetic methods is 1, 3-dipolar cycloaddition in which five-membered heterocyclic compounds are prepared by addition of 1, 3-dipolar compounds to double bonds.[84] Sulfur or phosphorus ylides as 1, 3-dipolephile are also useful starting materials for the synthesis of heterocycles,[69,70,79] although the mechanism of the reactions may be different from 1, 3-dipolar cycloaddition.

The reaction of 1, 4-dipoles with sulfur ylides would be expected to parallel

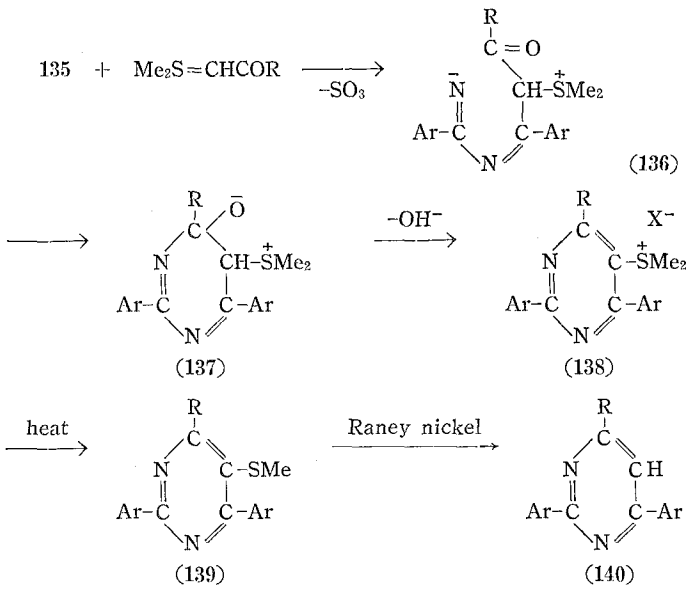


(135) (140)

the reaction of the 1, 4-dipole (**135**, a precursor) with 1, 3-dicarbonyl compounds in the presence of base,[85] while the mechanism of the reaction of carbonyl-stabilized sulfur ylides with 1, 3-dipoles is still not fully settled.

The authors have found that the reaction of carbonyl-stabilized sulfur ylides with **135**, a precursor of 1, 4-dipole, at ambient temperature furnished 5-dimethylsulfonium pyrimidines in 46–96% yields. (Table 30).

Chart 8.



Nucleophilic attack of the ylide on **135** and subsequent elimination of sulfur trioxide gives **136**. The ring closure of **136** to the betaine **137** is analogous one to the reaction of nitrile imine with sulfur ylide.[69] The elimination of hydroxy (or alkoxy) anion from **136** to the sulfonium salt **138** is feasible because of the

Table 30. Dimethylsulfonium Pyrimidines (138) and Methylthio Pyrimidines (139).

		138		139	
		Yield (%)	Mp. (°C)	Yield (%)	Mp. (°C)
a,	Ar=R=C_6H_5 X=$C_6H_5COCH_2SMe_2 \cdot SO_4$	77	145–151	32	111–113
b,	Ar=C_6H_5, R=*p*-$CH_3C_6H_4$ X=*p*-$CH_3C_6H_4COCH_2SMe_2 \cdot SO_4$	96	146–148	21	116–118
c,	Ar=C_6H_5, R=*p*-ClC_6H_4 X=*p*-$ClC_6H_4COCH_2SMe_2 \cdot SO_4$	93	155–158	53	126–128
d,	Ar=C_6H_5, R=*p*-BrC_6H_4 X=*p*-$BrC_6H_4COCH_2SMe_2 \cdot SO_4$	86	144–146	68	120–122
e,	Ar=C_6H_5, R=*m*-$NO_2C_6H_4$ X=*m*-$NO_2C_6H_4COCH_2SMe_2 \cdot SO_4$	46	128–131	96	121–122
f,	Ar=C_6H_5, R=β-Naphthyl X=β-Naphthyl-$COCH_2SMe_2 \cdot SO_4$	89	137–140	67	131–133
g,	Ar=C_6H_5, R=OH X=$Me_2SCH_2COOEt \cdot SO_4$	54	134–140	34	287–294

formation of resonance stabilized pyrimidine and drives the reaction to completion (Chart 8).

The structural assignment of **138** was substantiated by elemental analyses, IR, NMR and the decomposition in aqueous potassium chloride solution under heating to **139**.

Structure **139** was assigned on the basis of elemental, IR and NMR analyses. Desulfurization of **139 a** by Raney nickel gave 2, 4, 6-triphenyl pyrimidine which structure was characterized by comparison with authentic specimen.

In general the reaction was carried out by adding **135** to a solution of ylide **136** in benzene. The reaction mixture was kept at room temperature overnight. The precipitate from the reaction mixture was collected and washed with water to leave **138**.

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